



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of antiretroviral (ARV) agents for the treatment of HIV in adults and adolescents in the United States.
Panel members	The Panel is composed of approximately 50 voting members who have expertise in HIV care and research and includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are nongovernmental scientific members. The Panel also includes four to five community members with knowledge of HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open call for nominations. Each member serves on the Panel for a 4-year term with an option for reappointment for an additional term. See the Panel Roster for a list of current Panel members.
Financial disclosure	All members of the Panel submit a written financial disclosure annually, reporting any association with manufacturers of ARV drugs or diagnostics used to manage HIV infection. The latest version of the Financial Disclosure list is available on the AIDSinfo website.
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations in the guidelines are based on studies published in peer reviewed journals or data available in FDA drug labels. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2
Method of synthesizing data	Each section of the guidelines is assigned to a working group of Panel members with expertise in the section's area of interest. The working groups synthesize available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Recommendations endorsed by the Panel are included in the guidelines.
Other guidelines	<p>These guidelines focus on antiretroviral therapy (ART) for adults and adolescents with HIV. For a more detailed discussion on the use of ART in children and prepubertal adolescents (those with sexual maturity ratings of 1 to 3), clinicians should refer to the Pediatric Antiretroviral Guidelines.</p> <p>These guidelines also include a brief discussion on the management of women of reproductive age and pregnant women. For more details on the use of ARV drugs during pregnancy, see the Perinatal Guidelines.</p>
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency of dosing), new safety or efficacy data, or other information relating to ARV drugs that may have an impact on the clinical care of persons with HIV. In the event of new data of clinical importance, the Panel may post an interim announcement with recommendations on the AIDSinfo website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the AIDSinfo website .
Public comments	A 2-week public comment period follows the release of the updated guidelines on the AIDSinfo website. The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidinfo.nih.gov .

Table 2. Rating Scheme for Recommendations

Strength of Recommendation ⁱ	Quality of Evidence for Recommendation
A: Strong recommendation for the statement	I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B: Moderate recommendation for the statement	II: One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
C: Optional recommendation for the statement	III: Expert opinion

Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy^a (page 1 of 4)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation ^b or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed ^c
HIV Serology	√ If HIV diagnosis has not been confirmed								
CD4 Cell Count	√	√		√ During first 2 years of ART, or if viremia develops while patient is on ART, or if CD4 count is <300 cells/mm ³		√ After 2 Years on ART with Consistently Suppressed Viral Load CD4 Count 300–500 cells/mm ³ : • Every 12 months CD4 Count >500 cells/mm ³ : • CD4 monitoring is optional.	√	√	√ Every 3–6 months
HIV Viral Load	√	√	√ ^d	√ ^e	√ ^e		√	√	Repeat testing is optional.
Resistance Testing	√ ^f	√ ^f					√ ^f	√ ^f	√ ^f
HLA-B*5701 Testing		√ If considering ABC							
Tropism Testing		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist, or for patients experiencing virologic failure on a CCR5 antagonist-based regimen	√	

Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy^a (page 2 of 4)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation ^b or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed ^c
Hepatitis B Serology (HBsAb, HBsAg, HBcAb total) ^{g,h,i}	√	√ May repeat if patient is nonimmune and does not have chronic HBV infection ^h				√ May repeat if patient is nonimmune and does not have chronic HBV infection ^h		√ Including prior to starting HCV DAA (see HCV/HIV Coinfection)	
Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA) ^j	√					√ Repeat HCV screening for at-risk patients ^k		√	
Basic Chemistry^{l,m}	√	√	√		√			√	√ Every 6–12 months
ALT, AST, Total Bilirubin	√	√	√		√			√	√ Every 6–12 months
CBC with Differentialⁿ	√	√		√ When monitoring CD4 cell count; perform CBC cell count and CD4 concurrently		√ When no longer monitoring CD4 cell count		√	√ Every 3–6 months
Random or Fasting Lipid Profile^o	√	√				√		√	√ If normal at baseline, annually
Random or Fasting Glucose^p	√	√				√		√	√ If normal at baseline, annually

Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy^a (page 3 of 4)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation ^b or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed ^c
Urinalysis ^{m,q}	√	√			√ If on TDF ⁱ	√		√	
Pregnancy Test ^r	√	√						√	

^a This table pertains to laboratory tests done to select an ARV regimen and monitor for treatment responses or ART toxicities. Please refer to the [HIV Primary Care Guidelines](#) for guidance on other laboratory tests generally recommended for primary health care maintenance of HIV patients.¹

^b If ART is initiated soon after HIV diagnosis and entry into care, repeat baseline laboratory testing is not necessary.

^c ART is indicated for all individuals with HIV and should be started as soon as possible. However, if ART initiation is delayed, patients should be retained in care, with periodic monitoring as noted above.

^d If HIV RNA is detectable at 2–8 weeks, repeat testing every 4–8 weeks until viral load is suppressed to <200 copies/mL. Thereafter, repeat testing every 3–6 months.

^e In patients on ART, viral load typically is measured every 3–4 months. **More frequent monitoring may be considered in individuals who are having difficulties with ART adherence.** However, for adherent patients with consistently suppressed viral load and stable immunologic status for more than 2 years, monitoring can be extended to 6-month intervals.

^f Based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naïve persons should focus on testing for mutations in the reverse transcriptase and protease genes. If transmitted INSTI resistance is a concern or if a person presents with viremia while on an INSTI, providers should also test for resistance mutations to this class of drugs. In ART-naïve patients who do not immediately begin ART, repeat testing before initiation of ART is optional if resistance testing was performed at entry into care. In patients with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; see the section on [Drug Resistance Testing](#) for discussion of the potential limitations and benefits of proviral DNA assays in this situation. Results from prior resistance testing can be helpful in constructing a new regimen.

^g If patient has HBV infection (as determined by a positive HBsAg or HBV DNA test result), TDF or TAF plus either FTC or 3TC should be used as part of the ARV regimen to treat both HBV and HIV infections ([HBV/HIV](#)).

^h If HBsAg, HBsAb, and HBeAb test results are negative, hepatitis B vaccine series should be administered. Refer to the [HIV Primary Care Guidelines](#) and the [Adult and Adolescent Opportunistic Infection Guidelines](#) for detailed recommendations.^{1,2}

ⁱ Most patients with isolated HBeAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load test for confirmation. If the HBV viral load test is positive, the patient may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If the test is negative, the patient should be vaccinated. Refer to the [HIV Primary Care Guidelines](#) and the [Adult and Adolescent Opportunistic Infection Guidelines](#) for more detailed recommendations.^{1,2}

^j The HCV antibody test may not be adequate for screening in the setting of recent HCV infection (defined as acquisition within the past 6 months), or advanced immunodeficiency (CD4 count <100 cells/mm³). HCV RNA screening is indicated in persons who have been successfully treated for HCV or who spontaneously cleared prior infection. HCV antibody-negative patients with elevated ALT may need HCV RNA testing.

^k Injection drug users, persons with a history of incarceration, men with HIV who have unprotected sex with men, and persons with percutaneous/parenteral exposure to blood in unregulated settings are at risk of HCV infection.

Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy^a (page 4 of 4)

¹ Serum Na, K, HCO₃, Cl, BUN, creatinine, glucose, and creatinine-based estimated glomerular filtration rate. Serum phosphorus should be monitored in patients with chronic kidney disease who are on TDF-containing regimens.³

^m Consult the [Guidelines for the Management of Chronic Kidney Disease in HIV-Infected Patients: Recommendations of the HIV Medicine Association of the Infectious Diseases Society of America](#) for recommendations on managing patients with renal disease.³ More frequent monitoring may be indicated for patients with evidence of kidney disease (e.g., proteinuria, decreased glomerular dysfunction) or increased risk of renal insufficiency (e.g., patients with diabetes, hypertension).

ⁿ CBC with differential should be done when a CD4 count is performed. When CD4 count is no longer being monitored, the recommended frequency of CBC with differential is once a year. More frequent monitoring may be indicated for persons who are receiving medications that potentially cause cytopenia (e.g., ZDV, TMP-SMX).

^o If random lipids are abnormal, fasting lipids should be obtained. Consult the [2018 Guideline on the Management of Blood Cholesterol](#) for diagnosis and management of patients with dyslipidemia.⁴

^p If random glucose is abnormal, fasting glucose should be obtained. HbA1C is no longer recommended for diagnosis of diabetes in persons with HIV on ART (see the [ADA Guidelines](#)).⁵

^q Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens and monitored during treatment with these regimens.

^r For people of childbearing potential.

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CBC = complete blood count; CD4 = CD4 T lymphocyte; Cl = chloride; DAA = direct-acting antiviral; FTC = emtricitabine; HbA1C = hemoglobin A1c; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO₃ = bicarbonate; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine

Table 4. Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring^a

Clinical Scenario	Viral Load Monitoring	CD4 Count Monitoring
Before initiating ART	At entry into care (AIII) If ART initiation is deferred, repeat before initiating ART (AIII). In patients not initiating ART, repeat testing is optional (CIII).	At entry into care (AI) If ART is deferred, every 3 to 6 months ^b (AIII)
After initiating ART	Preferably within 2 to 4 weeks (and no later than 8 weeks) after initiation of ART (AIII); thereafter, every 4 to 8 weeks until viral load is suppressed (BIII).	3 months after initiation of ART (AIII)
After modifying ART because of drug toxicities or for regimen simplification in a patient with viral suppression	4 to 8 weeks after modification of ART to confirm effectiveness of new regimen (AIII).	Monitor according to prior CD4 count and duration on ART, as outlined below.
After modifying ART because of virologic failure	Preferably within 2 to 4 weeks (and no later than 8 weeks) after modification (AIII); thereafter, every 4 to 8 weeks until viral load is suppressed (BIII). If viral suppression is not possible, repeat viral load every 3 months or more frequently if indicated (AIII).	Every 3 to 6 months (AI)
During the first 2 years of ART	Every 3 to 4 months (AIII)	Every 3 to 6 months ^a (BII)
After 2 years of ART (VL consistently suppressed, CD4 consistently 300-500 cells/mm ³)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years (AIII).	Every 12 months (BII)
After 2 years of ART (VL consistently suppressed, CD4 consistently >500 cells/mm ³)		Optional (CIII)
While on ART with detectable viremia (VL repeatedly >200 copies/mL)	Every 3 months (AIII) or more frequently if clinically indicated (see Virologic Failure).	Every 3 to 6 months (AIII)
Change in clinical status (e.g., new HIV clinical symptom or initiation of interferon, chronic systemic corticosteroids, or antineoplastic therapy)	Every 3 months (AIII)	Perform CD4 count and repeat as clinically indicated ^c (AIII)

^a Monitoring of lymphocyte subsets other than CD4 (e.g., CD8, CD19) has not proven clinically useful, adds to costs, and is not routinely recommended (**BIII**).

^b Some experts may repeat CD4 count every 3 months in patients with low baseline CD4 count (<200–300 cells/mm³) before ART but every 6 months in those who initiated ART at higher CD4 cell count (e.g., >300 cells/mm³).

^c The following are examples of clinically indicated scenarios: changes in a patient's clinical status that may decrease CD4 count and thus prompt initiation of prophylaxis for opportunistic infections (OI), such as new HIV-associated symptoms, or initiation of treatment with medications which are known to reduce CD4 cell count.

Table 5. Recommendations for Using Drug-Resistance Assays (page 1 of 2)

Clinical Setting and Recommendation	Rationale
<u>In Acute or Recent (Early) HIV Infection:</u> Drug-resistance testing is recommended (AII). A genotypic assay is generally preferred (AIII). Treatment should not be delayed while awaiting results of resistance testing (AIII).	Drug-resistance testing can determine whether drug-resistant virus was transmitted. The initial regimen can be modified, if necessary, once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If ART is deferred, repeat resistance testing may be considered when therapy is initiated (CIII). A genotypic assay is generally preferred (AIII).	Repeat testing when ART is initiated may be considered because the patient may have acquired a drug-resistant virus (i.e., superinfection).
<u>In ART-Naive Patients with Chronic HIV:</u> Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART (AII). A genotypic assay is generally preferred (AIII).	Transmitted HIV with baseline resistance to at least 1 drug is seen in 10% to 17% of patients, and suboptimal virologic responses may be seen in patients with baseline resistant mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV.
For pregnant persons, or if ART will be initiated on the day of or soon after HIV diagnosis, treatment can be initiated prior to receiving resistance testing results.	If necessary, the ART regimen can be modified once resistance test results are available.
If an INSTI is considered for an ART-naive patient <u>and/or</u> transmitted INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay, which may need to be ordered separately (AIII).	Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTIs. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Currently, transmitted INSTI resistance is infrequent, but the risk of a patient acquiring INSTI-resistant strains may be greater in certain known exposure settings.
If therapy is deferred, repeat resistance testing may be considered before initiation of ART (CIII). A genotypic assay is generally preferred (AIII).	Repeat testing before initiation of ART may be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed (AI).	See Co-Receptor Tropism Assays section.
<u>In Patients with Virologic Failure:</u> Drug-resistance testing is recommended in patients on combination ART with HIV RNA levels >1,000 copies/mL (AI). In patients with HIV RNA levels >500 copies/mL but <1,000 copies/mL, testing may not be successful but should still be considered (BII).	Drug-resistance testing can help determine the role of resistance in drug failure and maximize the clinician's ability to select active drugs for the new regimen.
Resistance testing should be done while the patient is taking ART or, if that is not possible, within 4 weeks after ART discontinuation (AII). If >4 weeks have elapsed, resistance testing may still be useful to guide therapy; however, previously-selected mutations can be missed due to lack of drug selective pressure (CIII).	The absence of detectable resistance in such patients must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.
A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens and for those with noncomplex resistance patterns (AII).	Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant HIV.
All prior and current drug-resistance testing results should be reviewed and considered when designing a new regimen for a patient experiencing virologic failure (AIII).	Drug resistance mutations may decay with time, and mutations detected in prior resistance tests may not be detected in current tests, though they remain clinically relevant.
When virologic failure occurs while a patient is on an INSTI-based regimen, genotypic testing for INSTI resistance should be performed to determine whether to include drugs from this class in subsequent regimens (AII).	Genotypic assays provide information on resistance to NRTI-, NNRTI-, PI-, and INSTI-associated mutations. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory).

Table 5. Recommendations for Using Drug-Resistance Assays (page 2 of 2)

Clinical Setting and Recommendation	Rationale
Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns (BIII) .	Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns.
<u>In Patients with Suboptimal Suppression of Viral Load:</u> Drug-resistance testing is recommended in patients with suboptimal viral load suppression after initiation of ART (AII) .	Testing can determine the role of resistance in suboptimal viral suppression, and it can help the clinician identify the number of active drugs available in the current regimen and assess the need for a new regimen.
<u>In Pregnant Persons with HIV:</u> Genotypic resistance testing is recommended for all pregnant persons before initiation of ART (AIII) and for those entering pregnancy with detectable HIV RNA levels while on therapy (AI) .	The goals of ART in pregnant persons with HIV are to achieve maximal viral suppression for treatment of maternal HIV and to prevent perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal regimen for the patient. However, treatment should not be delayed while awaiting results of resistance testing. The initial regimen can be modified once resistance test results are available, if needed.
<u>In Patients with Undetectable Viral Load or Low-Level Viremia:</u> HIV-1 proviral DNA resistance assays may be useful in patients with HIV RNA below the limit of detection or with low-level viremia, where a HIV RNA genotypic assay is unlikely to be successful (CIII) .	This test may provide information about previously circulating resistant viral variants that are archived within proviral DNA. These assays may miss some or all prior resistance mutations that have occurred within the viral quasi-species, and therefore they should be interpreted with caution. The clinical utility of HIV-1 proviral DNA assays has not been fully determined.

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse-transcriptase inhibitors; NRTI = nucleoside reverse-transcriptase inhibitors; PI = protease inhibitor

Table 6a. Recommended Antiretroviral Regimens for Initial Therapy (page 1 of 2)

Selection of a regimen should be individualized based on virologic efficacy, potential adverse effects, childbearing potential and use of effective contraception, pill burden, dosing frequency, drug-drug interaction potential, comorbid conditions, cost, access, and resistance test results. Drug classes and regimens within each class are arranged first by evidence rating, and, when ratings are equal, in alphabetical order. Table 7 provides ARV recommendations based on specific clinical scenarios.

Recommended Initial Regimens for Most People with HIV
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.
<p>INSTI plus 2 NRTIs:</p> <p>Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.</p> <ul style="list-style-type: none"> • BIC/TAF/FTC (AI) • DTG/ABC/3TC (AI)—if HLA-B*5701 negative • DTG plus (TAF or TDF)^a plus (FTC or 3TC) (AI) • RAL plus (TAF or TDF)^a plus (FTC or 3TC) (BI for TDF/[FTC or 3TC], BII for TAF/FTC) <p>INSTI plus 1 NRTI:</p> <ul style="list-style-type: none"> • DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available
Recommended Initial Regimens in Certain Clinical Situations
These regimens are effective and tolerable but have some disadvantages when compared with the regimens listed above or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).
<p>INSTI plus 2 NRTIs:</p> <p>Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.</p> <ul style="list-style-type: none"> • EVG/c/(TAF or TDF)^a/FTC (BI) <p>Boosted PI plus 2 NRTIs:</p> <ul style="list-style-type: none"> • In general, boosted DRV is preferred over boosted ATV • (DRV/c or DRV/r) plus (TAF or TDF)^a plus (FTC or 3TC) (AI) • (ATV/c or ATV/r) plus (TAF or TDF)^a plus (FTC or 3TC) (BI) • (DRV/c or DRV/r) plus ABC/3TC —if HLA-B*5701 negative (BII) <p>NNRTI plus 2 NRTIs:</p> <ul style="list-style-type: none"> • DOR/TDF^a/3TC (BI) or DOR plus TAF^a/FTC (BIII) • EFV plus (TAF or TDF)^a plus (FTC or 3TC) <ul style="list-style-type: none"> • EFV 600 mg plus TDF plus (FTC or 3TC) (BI) • EFV 400 mg/TDF/3TC (BI) • EFV 600 mg plus TAF/FTC (BII) • RPV/(TAF or TDF)/FTC (BI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm³ <p>Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal:</p> <ul style="list-style-type: none"> • DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available • DRV/r plus RAL twice a day (CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm³ • DRV/r once daily plus 3TC^a (CI)
<p>Rating of Recommendations: A = Strong; B = Moderate; C = Optional</p>
<p>Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion</p>

^a TAF and TDF are two forms of TFV approved by FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Table 6a. Recommended Antiretroviral Regimens for Initial Therapy (page 2 of 2)

Note: The following are available as coformulated drugs: ABC/3TC, ATV/c, BIC/TAF/FTC, DOR/TDF/3TC, DRV/c, DRV/c/TAF/FTC, DTG/3TC, DTG/ABC/3TC, EFV (400 mg or 600 mg)/TDF/3TC, EFV/TDF/FTC, EVG/c/TAF/FTC, EVG/c/TDF/FTC, RPV/TAF/FTC, RPV/TDF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TFV = tenofovir; TDF = tenofovir disoproxil fumarate

Table 6b. Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors as Initial Therapy for Persons of Childbearing Potential

Background:

- Preliminary data from a study in Botswana suggested that there is an increased risk of NTDs (0.9%) in infants born to women who were receiving DTG at the time of conception.^{5,9} Updated results have shown that the prevalence of NTDs in infants who were exposed to DTG at the time of conception is lower (0.3%) than reported in the preliminary data, but still higher than in infants who were exposed to ART that did not contain DTG (0.1%).^{6,7}
- It is not yet known whether use of other INSTIs around the time of conception also poses a risk of NTDs (i.e., a class effect).
- There are insufficient data to determine whether use of BIC around the time of conception and during pregnancy is safe.
- There is limited data on RAL use around the time of conception. Thus far, based on data collected from the Antiretroviral Pregnancy Registry, the drug manufacturer, and in a cohort study from the United States and other countries, no case of NTD has been reported.¹⁰⁻¹² Among those receiving RAL during pregnancy, the rate of fetal malformations is within the expected range for pregnancy outcomes in the United States.¹⁰⁻¹²

Before Initiating an INSTI-Containing Regimen in a Person of Childbearing Potential:

- A pregnancy test should be performed (AIII).
- To enable individuals of childbearing potential to make informed decisions, providers should discuss the benefits and risks of using DTG around the time of conception, including the low risk of NTDs and the relative lack of information on the safety of using other commonly prescribed ARV drugs, including other INSTIs, around the time of conception (AIII).
- For individuals who are trying to conceive, the Panel recommends initiating one of the following regimens, which are designated as Preferred regimens during pregnancy in the Perinatal Guidelines: RAL, ATV/r or DRV/r plus TDF/FTC, TDF/3TC, or ABC/3TC. DTG would be an Alternative, rather than a Preferred, option (BII).
- For individuals who are not planning to conceive but who are sexually active and not using contraception, consider a regimen's effectiveness and tolerability, the available data on potential teratogenicity, and the person's preferences (e.g., low pill burden) when choosing among regimens recommended for initial therapy (Table 6a). In this situation, DTG would be an Alternative, rather than Preferred, option (BII). If the person becomes pregnant, changes to the ARV regimen may be warranted. Clinicians should refer to the [Perinatal Guidelines](#) for recommendations.
- For individuals who are using effective contraception, a DTG-based regimen is one of the recommended options; however, clinicians should discuss the risks and benefits of using DTG with patients to allow them to make an informed decision (AIII).
- An approach similar to that outlined for DTG should be considered for BIC-containing ART (AIII).
- EVG/c should not be used during pregnancy because of inadequate drug concentrations in the second and third trimesters (AII).
- Clinicians should refer to the [Perinatal Guidelines](#) when prescribing ART for a pregnant person with HIV.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ATV/r = atazanavir/ritonavir; BIC = bictegravir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; RAL = raltegravir; TDF = tenofovir disoproxil fumarate

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios
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This table guides clinicians in choosing an initial ARV regimen according to various patient and regimen characteristics and specific clinical scenarios. When more than one scenario applies to a person with HIV, clinicians should review considerations for each relevant scenario and use their clinical judgment to select the most appropriate regimen. This table is intended to guide the initial choice of regimen. However, if a person is doing well on a particular regimen, it is not necessary to switch to another regimen based on the scenarios outlined in this table. Please see Table 9 for additional information regarding the advantages and disadvantages of particular ARV medications. **Before initiating an INSTI-based regimen in a person of childbearing potential, review Table 6b for considerations in choosing the regimen.**

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm ³	Do Not Use the Following Regimens: <ul style="list-style-type: none"> • RPV-based regimens • DRV/r plus RAL 	A higher rate of virologic failure has been observed in those with low pretreatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 copies/mL)	Do Not Use the Following Regimens: <ul style="list-style-type: none"> • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL 	Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA levels
	HIV RNA >500,000 copies/mL	Do Not Use the Following Regimens: <ul style="list-style-type: none"> • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL • DTG/3TC 	For DTG/3TC, limited data are available in patients above this viral load threshold.
	HLA-B*5701 positive or result unknown	Do not use ABC-containing regimens.	ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.
	ARV should be started before HIV drug resistance results are available (e.g., in a person with acute HIV) or when ART is being initiated rapidly.	Avoid NNRTI-based regimens and DTG/3TC. Avoid ABC. Recommended ART Regimens: <ul style="list-style-type: none"> • BIC/TAF/FTC • DTG plus (TAF or TDF)^a plus (3TC or FTC) • (DRV/r or DRV/c) plus (TAF or TDF)^a plus (3TC or FTC) 	Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance. HLA-B*5701 results may not be available rapidly. Transmitted resistance to DRV, BIC , and DTG is rare, and these drugs have high barriers to resistance.
ART-Specific Characteristics	A one-pill, once-daily regimen is desired	STR Options as Initial ART Include: <ul style="list-style-type: none"> • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC 	Do not use DTG/ABC/3TC if patient is HLA-B*5701 positive. DTG/3TC is not recommended if HIV RNA is >500,000 copies/mL. Do not use DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection or unknown HBV status. Do not use RPV-based regimens if HIV RNA is >100,000 copies/mL and CD4 count is <200/mm ³ . See Appendix B, Table 10 for ARV dose recommendations in the setting of renal impairment.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios (page 2 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics, continued	Food effects	Regimens that Can be Taken Without Regard to Food: • BIC-, DOR-, DTG-, or RAL-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens that Should be Taken with Food: • ATV/r- or ATV/c-based regimens • DRV/r- or DRV/c-based regimens • EVG/c/TAF/FTC ^a • EVG/c/TDF/FTC ^a • RPV-based regimens	Food improves absorption of these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
		Regimens that Should be Taken on an Empty Stomach: • EFV-based regimens	Food increases EFV absorption and may increase CNS side effects.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	In general, avoid TDF. ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r). TAF may be used if CrCl >30 mL/min or if patient is on chronic hemodialysis (only studied with EVG/c/TAF/FTC). Consider avoiding ATV. ART Options When ABC, TAF, or TDF Cannot be Used: • DTG/3TC (if HIV RNA <500,000 copies/mL and without HBV coinfection) • DRV/r plus 3TC • DRV/r plus RAL (if CD4 count >200 cells/mm ³ and HIV RNA <100,000 copies/mL)	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 10 for specific dosing recommendations. TAF has less impact on renal function and lower rates of proteinuria than TDF. ATV has been associated with chronic kidney disease in some observational studies. ABC has not been associated with renal dysfunction.
	Liver disease with cirrhosis	Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.	Refer to Appendix B, Table 10 for specific dosing recommendations. Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.
	Osteoporosis	Avoid TDF.^a ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).	TDF is associated with decreases in BMD along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF ^a and ABC are associated with smaller declines in BMD than TDF.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios (page 3 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions , continued	Psychiatric illnesses	<p>Consider avoiding EFV- and RPV-based regimens.</p> <p>Patients on INSTI-based regimens who have pre-existing psychiatric conditions should be closely monitored.</p> <p>Some ARVs are contraindicated, and some psychiatric medications need dose adjustments when coadministered with certain ARVs.</p>	<p>EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality.</p> <p>INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series.</p> <p>See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.</p>
	HIV-associated dementia (HAD)	Avoid EFV-based regimens if possible.	The beneficial effects of ART on HAD-symptoms may be confounded by EFV-related neuropsychiatric effects.
	Medication-assisted treatment for opioid use disorder	<p>Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone.</p> <p>Clinical monitoring is recommended, as medications used to treat opioid dependence may need to be adjusted in some patients.</p>	<p>EFV reduces methadone concentrations and may lead to withdrawal symptoms.</p> <p>See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations.</p>
	Cardiac QTc interval prolongation	Consider avoiding EFV- or RPV-based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes.	High EFV or RPV concentrations may cause QT prolongation.
	High cardiac risk	<p>Consider avoiding ABC- and LPV/r -based regimens.</p> <p>If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen.</p> <p>Refer to Hyperlipidemia below for regimens associated with more favorable lipid profiles.</p>	<p>An increased risk of CV events with ABC has been observed in some studies.</p> <p>Observational cohort studies reported an association between some PIs (DRV, IDV, FPV, and LPV/r) and an increased risk of CV events; this risk has not been seen with ATV (see text). Further study is needed.</p> <p>Certain ART regimens are associated with more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking.</p>
	Hyperlipidemia	<p>The Following ARV Drugs Have Been Associated with Dyslipidemia:</p> <ul style="list-style-type: none"> • PI/r or PI/c • EFV • EVG/c <p>BIC, DOR, DTG, RAL, and RPV have fewer lipid effects.</p> <p>TDF lowers lipids; therefore, switching from TDF to TAF is associated with increased lipids.</p>	TDF has been associated with lower lipid levels than ABC or TAF.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios (page 4 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions , continued	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or BIC or DTG.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to Table 6b and the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
	Patients of childbearing potential who are planning to become pregnant or who are sexually active and not using effective contraception	Refer to Table 6b for further guidance.	
Presence of Coinfections	HBV infection	Use TDF or TAF, with FTC or 3TC If TDF and TAF Are Contraindicated: • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ART regimen (see HBV/HIV Coinfection).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV mutations can emerge rapidly when these drugs are used without another drug that is active against HBV.
	HCV treatment required	Refer to recommendations in HCV/HIV Coinfection , with special attention to potential interactions between ARV drugs and HCV drugs.	
	Treating TB disease with rifamycin antibiotics (rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug-drug interaction tables (Tables 21a-e) and TB/HIV Coinfection for information on ARV use with rifamycin antibiotics.	Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.

^a TAF and TDF are two FDA-approved forms of TFV. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BID = twice daily; BMD = bone mineral density; COBI = cobicistat; CD4 = CD4 T lymphocyte; CNS = central nervous system; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ESRD = end stage renal disease; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPV = fosamprenavir; FTC = emtricitabine; HAD = HIV-associated dementia; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options Recommended for Antiretroviral Therapy-Naïve Patients

Characteristics	ABC/3TC	3TC ^a	TDF/3TC	TAF/FTC	TDF/FTC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily	Once daily
Available Coformulations for ART-Naïve Patients	• ABC/3TC • DTG/ABC/3TC	DTG/3TC	• TDF/3TC • DOR/TDF/3TC • EFV 600 mg/TDF/3TC • EFV 400 mg/TDF/3TC	• TAF 25 mg/FTC • BIC/TAF 25 mg/FTC • DRV/c/TAF 10 mg/FTC • EVG/c/TAF 10 mg/FTC • RPV/TAF 25 mg/FTC	• TDF/FTC • EFV/TDF/FTC • EVG/c/TDF/FTC • RPV/TDF/FTC
Adverse Effects	ABC: • HSR to ABC is associated with the presence of HLA-B*5701 allele. • Increase in CV events is associated with ABC use in some, but not all, cohort studies.	See below	TDF: • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	TAF: • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF; similar to with ABC)	TDF: • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.
	3TC: No significant adverse effects			FTC: Skin discoloration	
Other Considerations	ABC: • Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient's allergy list. 3TC: • Epivir HBV™ is for the treatment of HBV and contains a different dose of 3TC than the formulation for ART. Thus, Epivir HBV™ should not be used for HIV treatment. • Coadministration of 3TC with sorbitol-containing drugs decreases 3TC concentration and should be avoided.			FTC should not be used as sole treatment for HBV due to development of resistance. Discontinuation may precipitate HBV flare if no other agents active against HBV are present.	
	3TC or ABC/3TC should not be used as treatment for HBV due to development of resistance. Discontinuation may precipitate HBV flare if no other agents active against HBV are present.			Also used for HBV treatment. Discontinuation may precipitate HBV flare. See Appendix B, Table 10 for dose recommendations in patients with renal insufficiency.	

^a 3TC is recommended for use with DTG in ART-naïve persons, and with DRV/r if ABC, TDF, and TAF are not optimal. Otherwise, dual-NRTI backbones are recommended.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended for Antiretroviral Therapy-Naïve Patients

Before starting an INSTI-based regimen in a person of childbearing potential, clinicians should refer to Table 6b for further guidance.

Characteristics	BIC	DTG	EVG	RAL
Dosing Frequency	Once daily	Once Daily: <ul style="list-style-type: none"> In ART-naïve or INSTI-naïve persons Twice Daily: <ul style="list-style-type: none"> If used with certain CYP3A4 and UGT1A1 inducers; or In INSTI-experienced persons with certain INSTI drug resistance mutations 	Once daily; requires boosting with COBI	<ul style="list-style-type: none"> 400 mg twice daily, or 1,200 mg (two 600-mg tablets) once daily
STR Available for ART-Naïve Patients	BIC/TAF/FTC	<ul style="list-style-type: none"> DTG/ABC/3TC DTG/3TC 	<ul style="list-style-type: none"> EVG/c/TAF/FTC EVG/c/TDF/FTC 	No
Available as a Single-Drug Tablet	No	Yes	No	Yes
Approved for ART-Experienced Patients	No	Yes, with twice-daily dosing for patients with certain INSTI drug resistance mutations	No, but sometimes used in combination with DRV and TAF/FTC as part of a simplification regimen in patients with resistance.	Yes, for patients with drug resistance mutations to RTV-boosted PIs or NNRTIs, but not to INSTIs
Virologic Efficacy Against EVG- or RAL-Resistant HIV	<i>In vitro</i> data indicate activity, but clinical trial data are not available.	Yes, for some isolates; effective with DTG 50 mg twice-daily dose	No	No
Adverse Effects	Nausea, diarrhea (GI disturbance greater with EVG/c), headache, insomnia. Among ARV-naïve individuals, initiation of INSTI-containing regimens has been associated with greater weight gain than NNRTI or boosted PI regimens (see text). Depression and suicidality are rare, occurring primarily in patients with pre-existing psychiatric conditions.			
	↑ CPK (4%)	Hypersensitivity, hepatotoxicity, ↑ CPK, myositis	↑ TG, ↑ LDL	↑ CPK, myopathy, hypersensitivity, SJS/TEN
CYP3A4 Drug-Drug Interactions	CYP3A4 substrate	CYP3A4 substrate (minor)	EVG is a CYP3A4 substrate; COBI is a CYP3A4 inhibitor	No
Chelation with Polyvalent Cation Supplements and Antacids	Oral absorption of all INSTIs may be reduced by polyvalent cations. See Table 21d for recommendations regarding dosing separation of INSTIs and these drugs.			
Other Key Potential Drug Interactions	UGT1A1 substrate, OCT2 and MATE1 inhibitor	P-gp substrate, UGT1A1 substrate	EVG is a UGT1A1 substrate; COBI is a P-gp inhibitor.	UGT1A1 substrate

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BID = twice daily; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; GI = gastrointestinal; INSTI = integrase strand transfer inhibitor; LDL = low density lipoprotein; MATE = multidrug and toxic compound extrusion; NNRTI = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; OAT = organic cation transporter; P-gp = p-glycoprotein; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; SJS/TEN = Stevens Johnson Syndrome/toxic epidermal necrolysis; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglyceride; UGT = uridine diphosphate glucuronosyltransferase

Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors that are Recommended for Antiretroviral Therapy-Naive Patients

Characteristics	DOR	EFV	RPV
Dosing Frequency	Once daily	Once daily	Once daily
Food Requirement	With or without food	On an empty stomach	With a meal
STR Available for ART-Naive Patients	DOR/TDF/3TC	<ul style="list-style-type: none"> • EFV 600 mg/TDF/FTC • EFV 600 mg/TDF/3TC • EFV 400 mg/TDF/3TC 	<ul style="list-style-type: none"> • RPV/TAF/FTC • RPV/TDF/FTC
Available as a Single-Drug Tablet	Yes	Yes	Yes
Adverse Effects	Generally well tolerated	<ul style="list-style-type: none"> • CNS side effects, including dizziness, abnormal dreams, headache, depression, suicidality, insomnia, somnolence • Skin rash • QTc prolongation 	<ul style="list-style-type: none"> • Depression, headache • Skin rash • QTc prolongation
CYP3A4 Drug-Drug Interactions	CYP3A4 substrate	CYP3A4 substrate, mixed inducer/inhibitor	CYP3A4 substrate
Other Significant Drug Interactions	None	CYP2B6 and 2C19 inducer	RPV oral absorption is reduced with increased gastric pH. Use of RPV with PPIs is not recommended; see Drug-Drug Interactions for dosing recommendations when RPV is coadministered with H2 blocker or antacids.

Key: 3TC = lamivudine; CNS = central nervous system; CYP = cytochrome P; DOR = doravirine; EFV = efavirenz; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 8d. Characteristics of Protease Inhibitor Options that are Recommended for Antiretroviral Therapy-Naive Patients

Characteristics	ATV	DRV
Dosing Frequency	Once daily	<ul style="list-style-type: none"> • Once daily for PI-naïve patients • Twice daily for PI-experienced patients with certain PI mutations
PK Boosting	PK-boosting with RTV or COBI is generally recommended. Unboosted ATV is also FDA-approved for ART-naïve patients.	DRV should only be used with a PK booster (i.e., RTV or COBI).
Fixed-Dose Formulation	<ul style="list-style-type: none"> • ATV/c 	<ul style="list-style-type: none"> • DRV/c • DRV/c/TAF/FTC
Available as a Single-Drug Tablet	Yes	Yes
Adverse Effects	<ul style="list-style-type: none"> • Jaundice • Indirect hyperbilirubinemia • Cholelithiasis • Nephrolithiasis • PR prolongation 	<ul style="list-style-type: none"> • Skin rash • Increase in serum transaminases • Hyperlipidemia • A higher cardiovascular risk was reported in participants taking DRV-based regimens than in those taking ATV-based regimens in an observational cohort study.
CYP3A4 Drug-Drug Interactions	CYP3A4 substrate, inhibitor	CYP3A4 substrate, inhibitor
Other Significant Drug Interactions	ATV absorption is reduced when ATV is given with acid-lowering therapies. See Table 21a for ATV dosing recommendations when the drug is coadministered with acid-lowering agents.	N/A

Key: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 1 of 5)

Note: All drugs within an ARV class are listed in alphabetical order.

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI Regimens	ABC/3TC	<ul style="list-style-type: none"> • Coformulated with DTG • Generic formulations are available for ABC/3TC, ABC, and 3TC. 	<ul style="list-style-type: none"> • May cause life-threatening HSRs in patients who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • In the ACTG 5202 study, patients with baseline HIV RNA $\geq 100,000$ copies/mL showed inferior virologic responses when ABC/3TC was given with EFV or ATV/r as opposed to TDF/FTC. This difference was not seen when ABC/3TC was used in combination with DTG. • ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.
	TAF/FTC	<ul style="list-style-type: none"> • Coformulated with BIC, DRV/c, EVG/c, or RPV • Active against HBV; a recommended dual-NRTI option for patients with HBV/HIV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC • Approved for patients with eGFR ≥ 30 mL/min • Can be used in patients with eGFR < 30 mL/min and on chronic hemodialysis 	<ul style="list-style-type: none"> • TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids. • Not recommended in pregnancy.
	TDF/3TC	<ul style="list-style-type: none"> • Coformulated with DOR • Generic formulations are available for TDF, 3TC, TDF/3TC, and EFV/TDF/3TC. • Long-term clinical experience • Active against HBV 	<ul style="list-style-type: none"> • Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters. • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
	TDF/FTC	<ul style="list-style-type: none"> • Coformulated with EFV, EVG/c, and RPV as STRs • Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection • Better virologic responses than ABC/3TC in patients with baseline viral loads $\geq 100,000$ copies/mL when combined with ATV/r or EFV • Associated with lower lipid levels than ABC or TAF 	<ul style="list-style-type: none"> • Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters. • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 2 of 5)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Single NRTI	3TC	<ul style="list-style-type: none"> • Coformulated with DTG as STR • Avoids potential toxicities associated with TDF, TAF, ABC 	<ul style="list-style-type: none"> • DTG/3TC is not recommended for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
INSTI	BIC	<ul style="list-style-type: none"> • Coformulated with TAF/FTC • Higher barrier to resistance than EVG and RAL • No food requirement 	<ul style="list-style-type: none"> • See Table 6b for considerations related to prescribing an INSTI-based regimen to people of childbearing potential. • Oral absorption of BIC can be reduced by simultaneous administration with drugs or supplements containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • Inhibits tubular secretion of Cr without affecting glomerular function. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug-drug interactions. • Should not be used in pregnancy because of lack of data and coformulation with TAF. • See discussion in text regarding weight gain related to INSTIs.
	DTG	<ul style="list-style-type: none"> • Higher barrier to resistance than EVG or RAL • Coformulated with ABC/3TC and 3TC • No food requirement • Minimal CYP3A4 interactions • Favorable lipid profile 	<ul style="list-style-type: none"> • Data from Botswana suggest that DTG exposure during conception may be associated with risk of NTDs in the infant (0.3% vs. 0.1% with non-DTG ARV drugs). • See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential. • Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function. • UGT1A1 substrate; potential for drug interactions (see Table 21d). • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions). • See discussion in text regarding weight gain related to INSTIs.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 3 of 5)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI, continued	EVG/c	<ul style="list-style-type: none"> • Coformulated with TDF/FTC or TAF/FTC • Compared with ATV/r, EVG/c causes smaller increases in total and LDL cholesterol. • EVG/c/TAF/FTC can be used in patients on chronic hemodialysis. 	<ul style="list-style-type: none"> • See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential. • EVG/c/TDF/FTC is only recommended for patients with baseline CrCl ≥ 70 mL/min; this regimen should be discontinued if CrCl decreases to < 50 mL/min. • COBI is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • Oral absorption of EVG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Has a lower barrier to resistance than boosted PI-, BIC-, or DTG-based regimens. • Food requirement. • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions). • Should not be used in pregnancy because of low drug exposure. • See discussion in text regarding weight gain related to INSTIs.
	RAL	<ul style="list-style-type: none"> • Compared to other INSTIs, has longest post-marketing experience • No food requirement • No CYP3A4 interactions • Favorable lipid profile 	<ul style="list-style-type: none"> • See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential. • Has a lower barrier to resistance than boosted PI-, BIC-, or DTG-based regimens. • Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported. • Rare cases of severe HSRs (including SJS and TEN) have been reported. • Higher pill burden than other INSTI-based regimens. • No FDC formulation. • Oral absorption of RAL can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • UGT1A1 substrate; potential for drug interactions (see Table 21d). • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions). • See discussion in text regarding weight gain related to INSTIs.
NNRTI	DOR	<ul style="list-style-type: none"> • Coformulated with TDF/3TC • Compared to EFV, fewer CNS side effects • No food requirement • Favorable lipid profile 	<ul style="list-style-type: none"> • Shorter-term clinical experience than with EFV and RPV. • Potential for CYP450 drug interactions (see Tables 21b, 22a and 22b). • Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 4 of 5)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
NNRTI, continued	EFV	<ul style="list-style-type: none"> • EFV 600 mg is coformulated with TDF/FTC and TDF/3TC. • EFV 400 mg is coformulated with TDF/3TC. • EFV 600-mg dose has long-term clinical experience and EFV-based regimens (except for EFV plus ABC/3TC) have well-documented efficacy in patients with high HIV RNA. • EFV 400 mg has fewer CNS side effects than EFV 600 mg. • EFV 600 mg can be given with rifamycin antibiotics (rifampin, rifabutin, or rifapentine). 	<ul style="list-style-type: none"> • Short- and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality and catatonia. Late onset ataxia and encephalopathy have also been reported. • Periodic screening for depression and suicidality is recommended in people with HIV who are taking a regimen that includes EFV. • Dyslipidemia • Rash • QTc interval prolongation; consider using an alternative to EFV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes. • Transmitted resistance is more common than with PIs and INSTIs. • Greater risk of resistance at the time of treatment failure than with PIs. • Potential for CYP450 drug interactions (see Tables 21b and 22a). • Should be taken on an empty stomach (food increases drug absorption and CNS toxicities).
	RPV	<ul style="list-style-type: none"> • Coformulated with TDF/FTC and TAF/FTC • RPV/TDF/FTC and RPV/TAF/FTC have smaller pill sizes than other coformulated ARV drugs • Compared with EFV: <ul style="list-style-type: none"> • Fewer CNS adverse effects • Fewer lipid effects • Fewer rashes 	<ul style="list-style-type: none"> • Not recommended in patients with pre-ART HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm³ because of higher rate of virologic failure in these patients. • Depression and suicidality • QTc interval prolongation; consider using an alternative to RPV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes. • Rash • Transmitted resistance is more common than with PIs and INSTIs. • More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and 2 NRTIs. • Potential for CYP450 drug interactions (see Tables 21b and 22a). • Meal requirement (>390 kcal) • Requires acid for adequate absorption. • Contraindicated with PPIs. • Use with H2 antagonists or antacids with caution (see Table 21a for detailed dosing information).
PIs	ATV/c or ATV/r	<ul style="list-style-type: none"> • Higher barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs. • ATV/c and ATV/r have similar virologic activity and toxicity profiles. • Observational cohort studies have found an association between some PIs (DRV, LPV/r, FPV, IDV) and an increased risk of CV events; this risk has not been seen with ATV. Further study is needed. See text for discussion. • Individual ATV and RTV components are available as generics. 	<ul style="list-style-type: none"> • Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice. • Food requirement • Absorption depends on food and low gastric pH (see Table 21a for interactions with H2 antagonists, antacids, and PPIs). • Nephrolithiasis, cholelithiasis, nephrotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a).

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 5 of 5)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
PIs, continued	ATV/c Specific considerations	Coformulated tablet	<ul style="list-style-type: none"> • COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF is not recommended in patients with CrCl <70 mL/min. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • COBI is not recommended in pregnancy because of low drug levels.
	DRV/c or DRV/r	<ul style="list-style-type: none"> • Higher barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs. 	<ul style="list-style-type: none"> • Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a). • Increased CV risk reported in one observational cohort study. • Hepatotoxicity has been reported, especially in those with pre-existing liver disease.
	DRV/c Specific considerations	• Coformulated as DRV/c and DRV/c/TAF/FTC	<ul style="list-style-type: none"> • COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF is not recommended in patients with CrCl <70 mL/min. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • COBI is not recommended in pregnancy because of low drug levels.

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; Mg = magnesium; MI = myocardial infarction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SJS = Stevens-Johnson syndrome; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrosis; UGT = uridine diphosphate glucuronosyltransferase

Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 1 of 2)

ARV Components or Regimens	Reasons for <u>Not</u> Recommending as Initial Therapy
NRTIs	
ABC/3TC/ZDV (Coformulated) As triple-NRTI combination regimen	<ul style="list-style-type: none"> • Inferior virologic efficacy
ABC/3TC/ZDV plus TDF As quadruple-NRTI combination regimen	<ul style="list-style-type: none"> • Inferior virologic efficacy
d4T plus 3TC	<ul style="list-style-type: none"> • Significant toxicities (including lipoatrophy, peripheral neuropathy) and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)
ddI plus 3TC (or FTC)	<ul style="list-style-type: none"> • Inferior virologic efficacy • Limited clinical trial experience in ART-naïve patients • ddI toxicities, such as pancreatitis and peripheral neuropathy
ddI plus TDF	<ul style="list-style-type: none"> • High rate of early virologic failure • Rapid selection of resistance mutations • Potential for immunologic nonresponse/CD4 cell decline • Increased ddI drug exposure and toxicities
ZDV/3TC	<ul style="list-style-type: none"> • Greater toxicities (including bone marrow suppression, GI toxicities, skeletal muscle myopathy, cardiomyopathy, and mitochondrial toxicities such as lipoatrophy, lactic acidosis, and hepatic steatosis) than recommended NRTIs
NNRTIs	
DLV	<ul style="list-style-type: none"> • Inferior virologic efficacy • Inconvenient (three times daily) dosing
ETR	<ul style="list-style-type: none"> • Insufficient data in ART-naïve patients
NVP	<ul style="list-style-type: none"> • Associated with serious and potentially fatal toxicity (hepatic events and severe rash, including SJS and TEN) • When compared to EFV, NVP did not meet noninferiority criteria
PIs	
ATV (Unboosted)	<ul style="list-style-type: none"> • Less potent than boosted ATV
DRV (Unboosted)	<ul style="list-style-type: none"> • Use without RTV or COBI has not been studied
FPV (Unboosted) or FPV/r	<ul style="list-style-type: none"> • Virologic failure with unboosted FPV-based regimen may result in selection of mutations that confer resistance to FPV and DRV • Less clinical trial data for FPV/r than for other RTV-boosted PIs
IDV (Unboosted)	<ul style="list-style-type: none"> • Inconvenient dosing (3 times daily with meal restrictions) • Fluid requirement • IDV toxicities, such as nephrolithiasis and crystalluria
IDV/r	<ul style="list-style-type: none"> • Fluid requirement • IDV toxicities, such as nephrolithiasis and crystalluria
LPV/r	<ul style="list-style-type: none"> • Higher pill burden than other PI-based regimens • Higher RTV dose than other PI-based regimens • GI intolerance
NFV	<ul style="list-style-type: none"> • Inferior virologic efficacy • Diarrhea
RTV as sole PI	<ul style="list-style-type: none"> • High pill burden • GI intolerance • Metabolic toxicity

Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 2 of 2)

ARV Components or Regimens	Reasons for <u>Not</u> Recommending as Initial Therapy
PIs, continued	
SQV (Unboosted)	<ul style="list-style-type: none"> • Inadequate bioavailability • Inferior virologic efficacy
SQV/r	<ul style="list-style-type: none"> • High pill burden • Can cause QT and PR prolongation; requires pretreatment and follow-up ECG
TPV/r	<ul style="list-style-type: none"> • Inferior virologic efficacy • Higher rate of adverse events than other RTV-boosted PIs • Higher dose of RTV required for boosting than other RTV-boosted PIs
Entry Inhibitors	
T-20 Fusion Inhibitor	<ul style="list-style-type: none"> • Only studied in patients with virologic failure • Twice-daily subcutaneous injections • High rate of injection site reactions
IBA CD4 Post-Attachment Inhibitor	<ul style="list-style-type: none"> • Only studied in a very small number of patients with virologic failure • Requires IV therapy • High cost
MVC CCR5 Antagonist	<ul style="list-style-type: none"> • Requires testing for CCR5 tropism before initiation of therapy • No virologic benefit when compared with other recommended regimens • Requires twice-daily dosing

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; CD4 = CD4 T lymphocyte; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DLV = delavirdine; DRV = darunavir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RTV = ritonavir; SJS = Stevens Johnson Syndrome; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 11. Antiretroviral Options for Patients with Virologic Failure

Designing a new regimen for patients who are experiencing treatment failure should always be guided by ARV history and results from current and past resistance testing. This table summarizes the text above and displays the most common or likely clinical scenarios seen in patients with virologic failure. For more detailed descriptions, please refer to the text above and/or consult an expert in drug resistance to assist in the design of a new regimen. It is also crucial to provide continuous adherence support to all patients before and after regimen changes.

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options ^{a,b}	Goal
First Regimen Failure	NNRTI plus two NRTIs	Most likely resistant to NNRTI +/- 3TC or FTC (i.e., NNRTI mutations +/- M184V/I). ^c Additional NRTI mutations may also be present.	Boosted PI plus two NRTIs (at least one active) (AIII) ; or DTG ^d plus two NRTIs (at least one active) (AI) ; or Boosted PI plus INSTI (AIII)	Resuppression
	Boosted PI plus two NRTIs	Most likely no resistance, or resistance only to 3TC or FTC (i.e., M184V/I, without resistance to other NRTIs) ^c	Continue same regimen (AI) ; or Another boosted PI plus two NRTIs (at least one active) (AI) ; or INSTI plus two NRTIs (at least one active; if only one of the NRTIs is fully active, or if adherence is a concern, DTG ^d is preferred over other INSTIs) (AIII) ; or Another boosted PI plus INSTI (BIII)	Resuppression
	INSTI plus two NRTIs	No INSTI resistance (can have 3TC or FTC resistance, i.e., only M184V/I, usually without resistance to other NRTIs) ^c	Boosted PI plus two NRTIs (at least one active) (AIII) ; or DTG ^d plus two NRTIs (at least one active) (AIII) ; or Boosted PI plus INSTI (BIII)	Resuppression
		EVG or RAL +/- 3TC or FTC resistance Resistance to first-line BIC or DTG is rare.	Boosted PI plus two NRTIs (at least one active) (AIII) ; or DTG ^{d,e} twice daily (if HIV is sensitive to DTG) plus two active NRTIs (AIII) ; or DTG ^{d,e} twice daily (if HIV is sensitive to DTG) plus a boosted PI (AIII) BIC has not been studied in this setting and cannot be recommended .	Resuppression
Second Regimen Failure and Beyond	Drug resistance with active treatment options	Use past and current genotypic +/- phenotypic resistance testing and ART history when designing new regimen.	At least two, and preferably three, fully active agents (AI) Partially active drugs may be used when no other options are available. Consider using an ARV drug with a different mechanism of action.	Resuppression

Table 11. Antiretroviral Options for Patients with Virologic Failure, continued

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options ^{a,b}	Goal
Second Regimen Failure and Beyond, continued	Multiple or extensive drug resistance with few treatment options	Use past and current genotypic and phenotypic resistance testing to guide therapy. Consider viral tropism assay when use of MVC is considered. Consult an expert in drug resistance, if needed.	Identify as many active or partially active drugs as possible based on resistance test results. Consider using an ARV drug with a different mechanism of action. Consider enrollment into clinical trials or expanded access programs for investigational agents, if available. Discontinuation of ARV drugs is not recommended.	Resuppression, if possible; otherwise, keeping viral load as low as possible and CD4 count as high as possible.
ART-Experienced Patients with Suspected Drug Resistance and Limited or Incomplete ARV and Resistance History	Unknown	Obtain medical records, if possible. Resistance testing may be helpful in identifying drug resistance mutations, even if the patient has been off ART. Keep in mind that resistance mutations may not be detected in the absence of drug pressure.	Consider restarting the old regimen, and obtain viral load and resistance testing 2–4 weeks after reintroduction of therapy. If no ARV history is available, consider initiating a regimen with drugs with high genetic barriers to resistance (e.g., DTG ^{d,e} and/or boosted DRV).	Resuppression

^a There are insufficient data to provide a recommendation for the continuation of 3TC or FTC in the presence of M184V/I.

^b When switching an ARV regimen in a patient with HBV/HIV coinfection, ARV drugs that are active against HBV should be continued as part of the new regimen. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.

^c If other NRTI resistance mutations are present, use resistance test results to guide NRTI usage in the new regimen.

^d Data from an observational study in Botswana suggest that there is an increased risk of NTDs in infants born to individuals who were receiving DTG at the time of conception; however, the risk of these defects is still low. Please refer to the discussion in the text and in [Table 6b](#) before prescribing DTG in persons of childbearing potential.

^e Response to DTG depends on the type and number of INSTI mutations.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; RAL = raltegravir

Table 12. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

Suspicion of Acute HIV Infection:

- Health care providers should consider the possibility of acute HIV infection in individuals with the signs, symptoms, or laboratory findings described below, and recent (within 2 to 6 weeks) high risk of exposure to HIV.^a
- Signs, symptoms, or laboratory findings of acute HIV infection may include but are not limited to one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.
- High-risk exposures include sexual contact with a person who has HIV or a person at risk of HIV infection; sharing needles and syringes to inject drugs, as well as equipment used to prepare drugs for injection; or any exposure in which an individual's mucous membranes or any breaks in the skin come in contact with bodily fluid that potentially carries HIV.

Differential Diagnosis:

- The differential diagnosis of acute HIV infection may include but is not limited to viral illnesses such as EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute or early HIV infection.

Testing to Diagnose/Confirm Acute HIV Infection:

- Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV antibody test result.
- A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.
- A negative or indeterminate HIV antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.
- A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be later confirmed by subsequent documentation of HIV antibody seroconversion.

ART After Diagnosis of Early HIV Infection:

- ART is recommended for all individuals with HIV, including those with early^a HIV infection **(AI)**. **ART should be initiated as soon as possible after HIV diagnosis (AII).**
- Once initiated, the goals of ART are to achieve sustained plasma virologic suppression and to prevent HIV transmission **(AII)**.
- All individuals of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII)**.
- Pregnant individuals with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV **(AI)**.
- A blood sample for genotypic drug resistance testing should be obtained before initiation of ART to guide the selection of the regimen **(AII)**, but ART should be initiated as soon as possible, often before resistance test results are available. If resistance is subsequently identified, treatment should be modified as needed.
- ART can be initiated before the results of drug resistance testing are known. In this setting, one of the following ART regimens is recommended **(AIII)**:
 - DTG with (TAF or TDF)^b plus (FTC or 3TC)
 - **BIC/TAF/FTC**
 - Boosted DRV with (TAF or TDF)^b plus (FTC or 3TC)
- **Pregnancy testing should be performed in individuals of childbearing potential before initiation of ART (AIII).**
- **Preliminary data from Botswana suggested that there is an increased risk of NTDs (0.9%) in infants born to women who were receiving DTG at the time of conception.⁴⁵ Follow-up data, however, showed that the prevalence of NTDs in association with DTG exposure at conception is lower (0.3%), but still slightly higher than with non-DTG containing ARV regimens (0.1%).^{46,47} Before initiating an INSTI-based regimen in a person of childbearing potential, clinicians should review Table 6b for information to consider when choosing an ART regimen.**

^a In some settings, behaviors that increase the risk of HIV infection may not be recognized or perceived as risky by the health care provider or the patient, or both. Thus, even in the absence of reported high-risk behaviors, symptoms and signs consistent with acute retroviral syndrome should motivate practitioners to consider a diagnosis of acute HIV infection.

^b TAF and TDF are two forms of TFV that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

Key: 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; **BIC = bicitgravir**; CMV = cytomegalovirus; DRV = darunavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 13. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction with ARV Drugs	Comments
Alcohol Use Disorder			
Acamprosate	666 mg PO three times a day or 333 mg PO three times a day for patients with CrCl 30–50 mL/min	No significant interaction with ARV drugs expected.	Contraindicated in patients with CrCl <30 mL/min.
Disulfiram	250 mg PO once daily	Use with caution when prescribing an ARV oral solution that contains ethanol and/or propylene glycol (e.g., FPV, LPV/r, RTV).	Counsel patients regarding disulfiram reaction when taken with alcohol; symptoms for the reaction may include flushing, tachycardia, nausea, vomiting, or hypotension.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Has the greatest efficacy of all FDA-approved medications for alcohol use disorder.
Opioid Use Disorder			
Buprenorphine	Individualize buprenorphine dosing based on a patient's opioid use. The dose range is 4–24 mg sublingually. Dosing is once daily or twice daily.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug-Drug Interactions for further recommendations.	Buprenorphine has 90% first pass hepatic metabolism. Verify that the patient is using the appropriate technique for sublingual administration before adjusting the dose, as improper administration will result in poor absorption and low drug levels.
Methadone	Individualize dose. Patients who receive higher doses (>100 mg) are more likely to remain in treatment.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug-Drug Interactions for further recommendations.	QTc prolongation is a concern at higher doses. Methadone can only be prescribed for OUD by a licensed OTP.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Longer time of continuous abstinence in those who received depot formulation naltrexone compared to placebo after transition from prison to community.
Nicotine Use Disorder			
Nicotine Replacement Therapy	There are a wide variety of FDA-approved nicotine replacement products. All formulations are effective.	No significant interaction with ARV drugs expected.	Work with the patient to identify the route of delivery that the patient will use and find most helpful.
Bupropion	Start at 150 mg PO daily for three days, then increase to either 150 mg twice daily or 300 mg once daily (only use formulations that are approved for once daily dosing).	Concentration may be reduced when used with ARV drugs that are CYP2D6 inducers. See Drug-Drug Interactions for further recommendations.	Tobacco quit date should ideally be 1 week after starting therapy.
Varenicline	Titrate dose based on tolerability until desired effect is achieved. The goal is to reach a dose of 1 mg PO twice daily. Requires dose adjustment in patients with CrCl <30 mL/min.	No significant interaction with ARV drugs expected.	Tobacco quit date should ideally be 1 week after starting therapy.

Key: ARV = antiretroviral; CrCl = creatinine clearance; CYP = cytochrome P; FDA = Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OUD = opioid use disorder; OTP = opioid treatment program; PO = orally; RTV = ritonavir; SR = sustained release

Table 14. Potential Interactions Between the Drugs Used in Gender-Affirming Hormone Therapy and Antiretroviral Drugs

Potential Effect on GAHT Drugs	ARV Drugs	GAHT Drugs that may be Affected by ARV Drugs	Clinical Recommendations for GAHT
ARV Drugs with the Least Potential to Impact GAHT Drugs	All NRTIs Entry Inhibitors: • IBA • MVC • T-20 Unboosted INSTIs: • BIC • DTG • RAL NNRTIs: • RPV • DOR	None	No dose adjustments necessary. Titrate dose based on desired clinical effects and hormone concentrations.
ARV Drugs that may Increase Concentrations of Some GAHT Drugs	EVG/c All boosted PIs	Dutasteride Finasteride Testosterone	Monitor patient for associated adverse effects; decrease the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.
ARV Drugs that may Decrease Concentrations of GAHT Drugs	PI/r NNRTIs: • EFV • ETR • NVP	Estradiol	Increase the dose of estradiol as needed to achieve the desired clinical effects and hormone concentrations.
	NNRTIs: • EFV • ETR • NVP	Dutasteride Finasteride Testosterone	Increase the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.
ARV Drugs with an Unclear Effect on GAHT Drugs	EVG/c PI/c	Estradiol	There is the potential for increased or decreased estradiol concentrations. Adjust the dose of estradiol to achieve the desired clinical effects and hormone concentrations.

Note: See Tables [21a](#), [21b](#), [21c](#), [21d](#), and [21e](#) for additional information regarding drug-drug interactions between ARV drugs and gender-affirming medications.

Key: ARV = antiretroviral; BIC = bictegravir; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; GAHT = gender-affirming hormone therapy; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; T-20 = enfuvirtide

Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 1 of 4)

The recommendations in this table for concomitant use of select HIV drugs with FDA-approved HCV DAA drugs are based on available PK interaction data or are predictions based on the known metabolic pathways of the agents. (Instances where PK interaction data are limited or not available are indicated in the table.) Whenever HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. As the field of HCV therapy is rapidly evolving, readers should also refer to the latest drug product labels and the [HCV Guidance](#) for updated information.

Note: Interactions with FPV, IDV, NFV, and SQV are **not** included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV PIs.

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents							
	NS5A Inhibitor	NS5B Inhibitor	Coformulated					
					SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT			
					(Cirrhosis classified as Child-Pugh class B or C)			
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI plus NS5B Inhibitor
	Daclatasvir	Sofosbuvir	Ledipasvir/Sofosbuvir	Sofosbuvir/Velpatasvir	Sofosbuvir/Velpatasvir/Voxilaprevir	Glecaprevir/Pibrentasvir	Elbasvir/Grazoprevir	Ombitasvir/Paritaprevir/RTV plus Dasabuvir ^a
NRTIs								
3TC	✓	✓	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓	✓	✓
TDF	✓	✓	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓	✓	✓
TAF	✓	✓	✓	✓	✓	✓	✓	✓
PIs								
Unboosted ATV	✓	✓	✓	✓	×	×	×	✓ ^b

Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 2 of 4)

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents							
	NS5A Inhibitor	NS5B Inhibitor	Coformulated					
			SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT					
			(Cirrhosis classified as Child-Pugh class B or C)					
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3A/4A PI	NS5A Inhibitor/NS3A/4A PI plus NS5B Inhibitor
Daclatasvir	Sofosbuvir	Ledipasvir/Sofosbuvir	Sofosbuvir/Velpatasvir	Sofosbuvir/Velpatasvir/Voxilaprevir	Glecaprevir/Pibrentasvir	Elbasvir/Grazoprevir	Ombitasvir/Paritaprevir/RTV plus Dasabuvir ^a	
PIs, continued								
ATV/r or ATV/c	✓ ↓ daclatasvir dose to 30 mg/day	✓	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events. ^d	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events. ^d	×	×	×	✓ ^c
DRV/r or DRV/c	✓	✓			✓ If a PI/r is used with TDF, ↑ TDF concentrations are expected. Monitor for TDF-associated adverse events. ^d Consider monitoring for hepatotoxicity. ^e	×	×	×
LPV/r	✓	✓			×	×	×	×
TPV/r	?	×	×	×	×	×	×	×
NNRTIs								
DOR	✓	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓	✓
EFV	✓ ↑ daclatasvir dose to 90 mg/day	✓		×	×	×	×	×
ETR	✓ ↑ daclatasvir dose to 90 mg/day	✓		×	×	×	×	×
NVP	✓ ↑ daclatasvir dose to 90 mg/day	✓		×	×	✓ ^f	×	×

Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 3 of 4)

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents							
	NS5A Inhibitor	NS5B Inhibitor	Coformulated					
			SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT					
			(Cirrhosis classified as Child-Pugh class B or C)					
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI	NS5A Inhibitor/NS3/4A PI plus NS5B Inhibitor
	Daclatasvir	Sofosbuvir	Ledipasvir/Sofosbuvir	Sofosbuvir/Velpatasvir	Sofosbuvir/Velpatasvir/Voxilaprevir	Glecaprevir/Pibrentasvir	Elbasvir/Grazoprevir	Ombitasvir/Paritaprevir/RTV plus Dasabuvir ^a
NNRTIs, continued								
RPV	✓	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓	×
INSTIs								
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓	✓	✓
DTG	✓	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓	✓
EVG/c/TDF/FTC	✓ ↓ daclatasvir dose to 30 mg/day	✓	×	✓ If used with TDF, monitor for TDF-associated adverse events.	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity. ^e	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity. ^g	×	×
EVG/c/TAF/FTC	✓ ↓ daclatasvir dose to 30 mg/day	✓	✓	✓	✓ Consider monitoring for hepatotoxicity. ^e	✓ Consider monitoring for hepatotoxicity. ^g	×	×
RAL	✓	✓	✓	✓	✓	✓	✓	✓
CCR5 Antagonist								
MVC	✓	✓	✓	✓	✓	✓	✓	×

Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 4 of 4)

^a Dasabuvir must be prescribed with ombitasvir/paritaprevir/RTV.

^b Reduce ATV dose to 300 mg and instruct the patient to take it in the morning at the same time as ombitasvir/paritaprevir/RTV plus dasabuvir. If RTV cannot be used, choose an alternative HCV regimen.

^c This HCV regimen contains RTV. If ATV is part of the ARV regimen, prescribe ATV 300 mg without COBI or RTV. The modified ARV regimen should be taken in the morning at the same time as ombitasvir/paritaprevir/RTV plus dasabuvir. Resume RTV or COBI regimen when HCV therapy is completed.

^d Consider using an alternative HCV treatment or ARV regimen to avoid increases in TDF exposure. If coadministration is necessary, monitor patient for TDF-associated adverse events.

^e Voxilaprevir exposures can increase when it is coadministered with pharmacologically boosted DRV or EVG. Until more safety data in clinical settings becomes available, patients who are receiving voxilaprevir and pharmacologically boosted DRV or EVG should be monitored for hepatotoxicity.

† Consider alternative ARV or HCV regimen. If used together, monitor for HCV efficacy.

^g Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data in clinical settings becomes available, patients who are receiving glecaprevir and EVG/c should be monitored for hepatotoxicity.

Key to Symbols:

✓ = ARV agents that can be used concomitantly

× = ARV agents not recommended

? = Data on PK interactions with ARV drug are limited or not available

↑ = Increase

↓ = Decrease

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; COBI = cobicistat; DAA = direct-acting antiviral agents; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPV = fosamprenavir; FTC = emtricitabine; HCV = hepatitis C virus; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Table 16. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 1 of 2)

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	<ul style="list-style-type: none"> • Care providers, nurses, social workers, case managers, pharmacists, and medication managers.
Strengthen early linkage to care and retention in care.	<ul style="list-style-type: none"> • Encourage health care team participation in linkage to and retention in care. • Use ARTAS training (if available).
Evaluate patient's knowledge about HIV infection, prevention, and treatment and, based on this assessment, provide HIV-related information.	<ul style="list-style-type: none"> • Keeping the patient's current knowledge base in mind, provide information about HIV, including the natural history of the disease, HIV viral load and CD4 count and expected clinical outcomes according to these parameters, therapeutic and prevention consequences of poor adherence, and importance of staying in HIV care.
Identify facilitators, potential barriers to adherence, and necessary medication management skills both before starting ART and on an ongoing basis.	<ul style="list-style-type: none"> • Assess patient's cognitive competence and impairment. • Assess behavioral and psychosocial challenges, including depression, mental illnesses, levels of social support, levels of alcohol consumption and current substance use, nondisclosure of HIV serostatus, and stigma. • Identify and address language and literacy barriers. • Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence). • Ask about medication-taking skills and foreseeable challenges with adherence (e.g., past difficulty keeping appointments, adverse effects from previous medications, issues managing other chronic medications, need for medication reminders and organizers). • Assess structural issues, including unstable housing, lack of income, unpredictable daily schedule, lack of prescription drug coverage, lack of continuous access to medications, transportation problems.
Provide needed resources.	<ul style="list-style-type: none"> • Provide or refer for mental health and/or substance abuse treatment. • Provide resources to obtain prescription drug coverage (e.g., Common Patient Assistance Program Application (CPAPA): http://bit.ly/CommonPAPForm; Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs: http://bit.ly/1XlahvN) • Provide resources about stable housing, social support, transportation assistance, and income and food security.
Involve the patient in ARV regimen selection.	<ul style="list-style-type: none"> • Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence. • Assess daily activities and tailor regimen to predictable and routine daily events. • Consider preferential use of PI/r-based or DTG-based ART if poor adherence is anticipated. • Consider use of STR formulations. • Assess if cost/copayment for drugs will affect adherence and access to medications.
Assess adherence at every clinic visit.	<ul style="list-style-type: none"> • Monitor viral load as a strong biologic measure of adherence. • Use a simple behavioral rating scale or self-reported assessment. • Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or "white-coat adherence" responses. • Ensure that other members of the health care team also assess and support adherence.
Use positive reinforcement to foster adherence success.	<ul style="list-style-type: none"> • Inform patients of low or nondetectable levels of HIV viral load and increases in CD4 cell counts. • Thank patients for attending their appointments.

Table 16. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 2 of 2)

Strategies	Examples
Identify the type of and reasons for poor adherence and target ways to improve adherence.	<ul style="list-style-type: none"> • Failure to understand dosing instructions. • Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy). • Pill aversion or pill fatigue. • Adverse effects. • Inadequate understanding of drug resistance and its relationship to adherence. • Patient is unaware of appointments or appointments are not scheduled with proper patient input. • Cost-related issues (copays for medications or visits, missed work time). • Depression, drug and alcohol use, homelessness, poverty. • Stigma of taking pills or attending HIV-related appointments. • Nondisclosure of status leading to missed doses, refills, or appointments.
Select from among available effective adherence and retention interventions.	<ul style="list-style-type: none"> • See https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html for a summary of best practice interventions to improve linkage, retention, and adherence. • Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms). • Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance). • Use patient prescription assistance programs (see above, under “Provide needed resources”). • Use motivational interviews. • Provide outreach for patients who drop out of care • Use peer or paraprofessional treatment navigators. • Recognize positive clinical outcomes resulting from better adherence. • Arrange for DOT in persons in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (reminder calls, flexible scheduling, open access, active referrals, and improved patient satisfaction).
Systematically monitor retention in care.	<ul style="list-style-type: none"> • Record and follow up on missed visits.

Key to Acronyms: ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; CD4 = CD4 T lymphocyte; DOT = directly observed therapy; DTG = dolutegravir; PI/r = ritonavir-boosted protease inhibitor; STR = single tablet regimen

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 1 of 5)

Adverse effects for ARV drugs that are no longer commonly used in clinical practice (ddI, d4T, FPV/r, IDV, NFV, SQV/r, and TPV/r) have been removed from this table, with the exception of lipodystrophy and peripheral neuropathy associated with ddI and d4T. Because these effects may persist long after discontinuation of ddI or d4T, and patients may still present with these long-lasting toxicities, the drugs remain listed among the ARVs associated with these two effects. Refer to the product labels or to the July 10, 2019, version of the guidelines (found in the archived guidelines section of *AIDSinfo*) for information regarding the adverse effects associated with these older ARVs.

This table focuses on ARV-associated adverse effects that a patient may experience as a result of taking an ARV regimen. For information regarding potential adverse effects of ARVs on fetuses and newborns when certain ARVs are taken around the time of conception or during pregnancy, refer to Table 6b and to the [Perinatal Guidelines](#).

In this table, N/A indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See [Appendix B, Tables 3-9](#) for additional information listed by drug.

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Bone Density Effects	<p>TDF: Associated with greater loss of BMD than other NRTIs, especially when given with a PK booster. Osteomalacia may be associated with renal tubulopathy and urine phosphate wasting.</p> <p>TAF: Associated with smaller declines in BMD than those seen with TDF.</p>	Decreases in BMD observed after the initiation of any ART regimen.			N/A
Bone Marrow Suppression	ZDV: Anemia, neutropenia	N/A	N/A	N/A	N/A
Cardiac Conduction Effects	N/A	RPV, EFV: QTc prolongation	ATV/r and LPV/r: PR prolongation. Risk factors include pre-existing heart disease and concomitant use of medications that may cause PR prolongation.	N/A	N/A
Cardiovascular Disease	ABC: Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in patients with traditional CVD risk factors.	N/A	Boosted DRV and LPV/r: Associated with cardiovascular events in some cohorts	N/A	N/A

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 2 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Cholelithiasis	N/A	N/A	ATV: Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months after ARV initiation.	N/A	N/A
Diabetes Mellitus and Insulin Resistance	ZDV	N/A	LPV/r, but not with boosted ATV or DRV	N/A	N/A
Dyslipidemia	ZDV > ABC: ↑ TG and ↑ LDL TAF: ↑ TG, ↑ LDL, and ↑ HDL (no change in TC:HDL ratio) TDF has been associated with lower lipid levels than ABC or TAF.	EFV: ↑ TG, ↑ LDL, ↑ HDL	All RTV- or COBI-Boosted PIs: ↑ TG, ↑ LDL, ↑ HDL LPV/r > DRV/r and ATV/r: ↑ TG	EVG/c: ↑ TG, ↑ LDL, ↑ HDL	N/A
Gastrointestinal Effects	ZDV > Other NRTIs: Nausea and vomiting	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting) LPV/r > DRV/r and ATV/r: Diarrhea	EVG/c: Nausea and diarrhea	IBA: In a study of 40 people, 8% of patients reported diarrhea.
Hepatic Effects	When TAF, TDF, 3TC, and FTC are withdrawn in Patients with HBV/ HIV Coinfection or when HBV Resistance Develops: Patients with HBV/HIV coinfection may develop severe hepatic flares. ZDV: Steatosis	EFV: Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. A 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 counts >250 cells/mm ³ and men with pre-NVP CD4 counts >400 cells/mm ³ . NVP should never be used for post-exposure prophylaxis. EFV and NVP are not recommended in patients with hepatic insufficiency (Child-Pugh class B or C).	All PIs: Drug-induced hepatitis and hepatic decompensation have been reported. ATV: Jaundice due to indirect hyperbilirubinemia	DTG: Persons with HBV or HCV coinfection may be at higher risk of DTG-associated hepatotoxicity.	MVC: Hepatotoxicity with or without rash or HSRs reported.

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 3 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Hypersensitivity Reaction Excluding rash alone or Stevens-Johnson syndrome	ABC: Contraindicated if patient is HLA-B*5701 positive. Median onset for HSR is 9 days after treatment initiation; 90% of reactions occur within 6 weeks. HSR Symptoms (in Order of Descending Frequency): Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms Symptoms worsen with continuation of ABC. Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.	NVP: Hypersensitivity syndrome of hepatotoxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, renal dysfunction, granulocytopenia, or lymphadenopathy. Risk is greater for ARV-naïve women with pre-NVP CD4 counts >250 cells/mm ³ and men with pre-NVP CD4 counts >400 cells/mm ³ . Overall, risk is higher for women than men. A 2-week dose escalation of NVP reduces risk.	N/A	RAL: HSR reported when RAL is given with other drugs also known to cause HSRs. All ARVs should be stopped if HSR occurs. DTG: Reported in <1% of patients in clinical development program	MVC: HSR reported as part of a syndrome related to hepatotoxicity.
Lactic Acidosis	Reported with Older NRTIs, d4T, ZDV, and ddI , but not with ABC, 3TC, FTC, TAF, or TDF.	N/A	N/A	N/A	N/A
Lipodystrophy	Lipoatrophy: Associated with history of exposure to d4T or ZDV (d4T > ZDV). Not reported with ABC, 3TC or FTC, TAF or TDF.	Lipohypertrophy: Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.			N/A
Myopathy/ Elevated Creatine Phosphokinase	ZDV: Myopathy	N/A	N/A	RAL and DTG: ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.	N/A

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 4 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Nervous System/ Psychiatric Effects	History of Exposure to ddI, ddC, or d4T: Peripheral neuropathy (can be irreversible)	<p>Neuropsychiatric Events: EFV > RPV, DOR, ETR</p> <p>EFV: Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation, ataxia, encephalopathy. Some symptoms may subside or diminish after 2–4 weeks. Bedtime dosing and taking without food may reduce symptoms. Risk factors include psychiatric illness, concomitant use of agents with neuropsychiatric effects, and genetic factors.</p> <p>RPV: Depression, suicidality, sleep disturbances</p> <p>DOR: Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality and self-harm</p>	N/A	All INSTIs: Insomnia, depression, and suicidality have been reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.	N/A
Rash	FTC: Hyperpigmentation	All NNRTIs	ATV, DRV, and LPV/r	All INSTIs	MVC, IBA
Renal Effects/ Urolithiasis	<p>TDF: ↑ SCr, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk.</p> <p>TAF: Less impact on renal biomarkers and lower rates of proteinuria than TDF.</p>	RPV: Inhibits Cr secretion without reducing renal glomerular function.	<p>ATV and LPV/r: Associated with increased risk of chronic kidney disease in a large cohort study.</p> <p>ATV: Stone or crystal formation. Adequate hydration may reduce risk.</p> <p>COBI (as a Boosting Agent for DRV or ATV): Inhibits Cr secretion without reducing renal glomerular function.</p>	DTG, COBI (as a Boosting Agent for EVG), and BIC: Inhibits Cr secretion without reducing renal glomerular function	IBA: SCr abnormalities ≥Grade 3 reported in 10% of trial participants.

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 5 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Stevens-Johnson Syndrome/ Toxic Epidermal Necrosis	N/A	NVP > EFV, ETR, RPV	Some reported cases for DRV, LPV/r, and ATV	RAL	N/A
Weight Gain	Weight gain has been associated with initiation of ART and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV.			INSTI > other ARV drug classes	N/A

Key: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; Cr = creatinine; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; ddl = didanosine; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 18. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents (page 1 of 3)

This table focuses on ARV-associated adverse effects that patients may experience as a result of a current ARV regimen. For information regarding ARV choices to use in individuals of childbearing potential and during pregnancy to avoid potential ARV adverse effects on fetuses and newborns refer to [Table 6b](#) and to the [Perinatal Guidelines](#).

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Bone Density Effects	TDF ^a	TAF or ABC ^b NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate.	Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain. TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.
Bone Marrow Suppression	ZDV	Regimen not including ZDV	ZDV has been associated with neutropenia and macrocytic anemia.
Calculi Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if ATV is the presumed cause of the calculi.
Cardiac QTc Interval Prolongation	EFV, RPV	Boosted ATV or DRV, DOR , or INSTI-based regimen	High EFV and RPV exposures may cause QT prolongation. Consider switching from EFV- or RPV-based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes.
Cardiovascular Events Myocardial infarction, ischemic stroke	ABC	TDF or TAF	ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.
	RTV- or COBI-boosted PI regimens, EFV	RAL, DTG, BIC, RPV, or DOR	If lipids are a concern, see Dyslipidemia below. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.
Dyslipidemia Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted EFV-based regimens	BIC, DTG, RAL, DOR , or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r. ^c
Gastrointestinal Effects Nausea, diarrhea	LPV/r	Boosted ATV or DRV, INSTI, NNRTI	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant ARV substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	BIC, DTG, RAL, or NNRTI	In a trial of treatment-naïve patients, rates of diarrhea and nausea were similar for EVG/c/TDF/FTC and ATV/r plus TDF/FTC.

Table 18. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents (page 2 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Hypersensitivity Reaction	ABC	Any appropriate ABC-sparing regimen	Never rechallenge with ABC following a suspected HSR, regardless of the patient's HLA-B*5701 status.
	EFV, ETR, NVP, RPV	Non-NNRTI ART	Risk of HSR with NVP is higher for women and those with high CD4 counts.
	DTG, RAL	Non-INSTI ART	Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.
	MVC	Suitable alternative ART	
Insulin Resistance	LPV/r	INSTI, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r on insulin resistance. However, traditional risk factors for insulin resistance may be stronger risk factors than the use of any PI.
Jaundice and Icterus	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	Increases in unconjugated bilirubin are common with ATV and generally do not require modification of therapy unless resultant symptoms are distressing to the patient.
Lipoatrophy	Peripheral lipoatrophy (loss of subcutaneous fat of the limbs, face, and buttocks) is associated with prior thymidine analog (d4T and ZDV) use. Despite switching from these ARVs, fat recovery remains slow (may take years) and incomplete.		
Lipohypertrophy	Accumulation of visceral, truncal, dorsocervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse lipohypertrophy.		
Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression, ataxia, encephalopathy	EFV, RPV	DOR , ETR, PI/c, or PI/r INSTIs may be used, but monitoring is recommended (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug, but in some patients, ataxia or encephalopathy may appear months to years after EFV-initiation. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
Rash	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	Mild rashes that develop after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	Mild rashes following DRV/r use may resolve without modification of therapy. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF ^a	ABC, ^b TAF (for patients with CrCl >30 mL/min, unless on chronic hemodialysis), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.	TDF may cause tubulopathy. Switching from TDF to TAF is associated with improvement in proteinuria and renal biomarkers. The long-term impact of TAF on patients with pre-existing renal disease, including overt proximal tubulopathy, is unknown, and close clinical monitoring is recommended in this setting.
	ATV/c, ATV/r, LPV/r	BIC, DTG, EVG/c/TAF/FTC, RAL, boosted DRV, or NNRTI	COBI, DTG, BIC, and, to a lesser extent, RPV, can increase SCr through inhibition of creatinine secretion. This effect does not affect glomerular filtration. However, assess patient for renal dysfunction if SCr increases by >0.4 mg/dL.

Table 18. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agents (page 3 of 3)

^a In patients with chronic active HBV infection, another agent that is active against HBV should be substituted for TDF.

^b ABC should be used only in patients known to be HLA-B*5701 negative.

^c TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

Table 19a. Insurance and Health Program Prescription Drug Pricing and Access (page 1 of 2)

Insurance/Health Program	Prescription Drug Pricing and Access
Medicaid	<p>Drug manufacturers must participate in MDRP for their drugs to be covered by Medicaid and under Medicare Part B.</p> <p>Manufacturers are required to pay Medicaid programs a rebate of at least 23.1% of the average price paid to manufacturers by wholesalers (AMP) for most brand-name drugs sold to retail pharmacies (13% for generics). Manufacturers pay additional rebates if this confidential AMP increases faster than the CPI-U rate of inflation.</p> <p>States are permitted to require “nominal” cost-sharing for medical and pharmacy benefits for some beneficiaries though many elect not to do so. States can obtain a waiver to allow them to apply higher cost-sharing.</p>
Medicare	<p>ARVs are one of six “protected drug classes” under Medicare Part D. Part D plans must provide access to all, or substantially all, FDA-approved ARVs. Part D plan sponsors, or PBMs on their behalf, negotiate rebates on outpatient drugs with manufacturers; the extent of rebating is unclear.</p> <p>Most physician-administered drugs and biologics are covered under Medicare Part B at a set cost: ASP plus 6%. This pricing mechanism controls spending by narrowing the spread between what is actually paid for the drug and what is actually billed to Medicare.</p> <p>Premiums and cost-sharing payments may be significant for both services and prescription drugs; there is no cap on out-of-pocket spending under Part A (hospital care) and Part B.</p> <p>Some subsidies and supplemental coverage are offered for low-income beneficiaries. Manufacturer copay assistance programs cannot be applied to Part B or Part D cost sharing; cost sharing support is available from ADAPs, foundations, and other sources, based on financial eligibility criteria.</p>
Commercial Insurance	<p>Private insurance plans, or PBMs on their behalf, negotiate rebates on inpatient and outpatient drugs with manufacturers; the extent of rebating is unclear.</p> <p>Formulary restrictions and utilization management (prior authorization, step therapy, higher cost sharing) are possible as cost-containment measures.</p> <p>Cost sharing can be highly variable. Manufacturer copay assistance programs can be applied in most cases but may not count toward annual Affordable Care Act cost sharing limits; cost sharing support is also available from ADAPs, foundations, and other sources based on financial eligibility criteria.</p>

Table 19a. Insurance and Health Program Prescription Drug Pricing and Access (page 2 of 2)

Insurance/Health Program	Prescription Drug Pricing and Access
ADAPs	<p>Significant discounting on most ARVs negotiated by the ADAP Crisis Task Force is allowed under the 340B Drug Pricing Program.</p> <p>There is usually no cost sharing for ADAP clients who are uninsured. ADAP can assist with commercial or public insurance out-of-pocket costs.</p>
Veterans Affairs	<p>The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the “Big Four”): The Department of Veterans Affairs, the Department of Defense, the Public Health Service (including the Indian Health Service), and the Coast Guard. The FCP of a drug includes a 24% discount on a drug’s average price paid by non-federal purchasers. Additional discounts may be applied if non-federal purchase prices increase faster than the CPI-U inflation rate.</p> <p>Big Four prices may be 40% to 50% below list prices. VA may negotiate further price reductions.</p> <p>Prescription drug cost sharing is generally nominal; medications are not withheld from those who cannot afford cost sharing expenses.</p>
Community Health Centers	<p>Many community health centers are enrolled in the 340B Drug Pricing Program, which allows for discounted drug purchasing using the MDRP formula.</p> <p>Discounts start at 23.1% off AMP, with additional discounts if the AMP increases faster than the CPI-U rate of inflation.</p> <p>Cost-sharing in community health centers is first driven by payer source. For clients who are uninsured, cost-sharing, if required, is typically based on a sliding fee scale.</p>

Key: ADAP = AIDS Drug Assistance Programs; AMP = average manufacturer price; ARV = antiretroviral; ASP = average sales price; CPI-U = consumer price index-urban; FCP = Federal Ceiling Price; FDA = Food and Drug Administration; MDRP = Medicaid Drug Rebate Program; PBM = pharmacy benefits manager; VA = Veterans Affairs

Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 5)

Table 19b includes three benchmark prices, rounded to the nearest dollar, for commonly used ARV drugs^a as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact patients' pharmacies or payers regarding actual prices, comparative cost savings, formulary restrictions, and patient cost-sharing requirements.

Wholesale acquisition cost (WAC) is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs, as these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs among wholesalers and pharmacies decrease substantially. **Average wholesale price (AWP)** has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP include variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the Veterans' Administration), pharmacy benefit managers (PBMs), commercial insurers, Medicaid, 340B pharmacies, and AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum prices are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the Food and Drug Administration. This federally established price is the **federal upper limit (FUL)**. Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); commercial insurers set their own reimbursement upper limits with pharmacies. Whereas WACs and AWP are generally set annually, FULs are adjusted on a monthly basis, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In the table below, the FUL for a drug is described as "pending" if a generic drug currently lacks the competition required to trigger a FUL.

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) ^b	AWP (Monthly) ^b	FUL (As of Oct. 31, 2019) ^c
NRTIs					
Abacavir					
• Generic	300 mg tablet	60 tablets	\$150 to \$482	\$502 to \$603	\$43
• Ziagen	300 mg tablet	60 tablets	\$559	\$670	
Emtricitabine					
• Emtriva	200 mg capsule	30 capsules	\$537	\$644	N/A
Lamivudine					
• Generic	300 mg tablet	30 tablets	\$75 to \$343	\$324 to \$430	\$51
• Epivir	300 mg tablet	30 tablets	\$416	\$499	
Tenofovir Disoproxil Fumarate					
• Generic	300 mg tablet	30 tablets	\$27 to \$163	\$110 to \$1,216	\$203
• Viread	300 mg tablet	30 tablets	\$1,196	\$1,435	

Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) ^b	AWP (Monthly) ^b	FUL (As of Oct. 31, 2019) ^c
NRTIs, continued					
Zidovudine					
• Generic	300 mg tablet	60 tablets	\$36 to \$54	\$54 to \$365	\$13
NRTI Combination Products					
Abacavir/Lamivudine					
• Generic	600 mg/300 mg tablet	30 tablets	\$185 to \$1,116	\$1,393 to \$1,550	\$182
• Epzicom	600 mg/300 mg tablet	30 tablets	\$1,292	\$1,550	
Tenofovir Alafenamide/Emtricitabine					
• Descovy	25 mg/200 mg tablet	30 tablets	\$1,758	\$2,109	N/A
Tenofovir Disoproxil Fumarate/Emtricitabine					
• Truvada	300 mg/200 mg tablet	30 tablets	\$1,676	\$2,011	N/A
Tenofovir Disoproxil Fumarate/Lamivudine					
• Cimduo	300 mg/300 mg tablet	30 tablets	\$1,005	\$1,207	N/A
• Temixys	300 mg/300 mg tablet	30 tablets	\$850	\$1,020	N/A
Zidovudine/Lamivudine					
• Generic	300 mg/150 mg tablet	60 tablets	\$134 to \$578	\$878 to \$932	\$123
• Combivir	300 mg/150 mg tablet	60 tablets	\$901	\$1,082	
Abacavir Sulfate/Zidovudine/Lamivudine					
• Generic	300 mg/300 mg/150 mg tablet	60 tablets	\$1,391	\$1,738	Pending
• Trizivir	300 mg/300 mg/150 mg tablet	60 tablets	\$1,610	\$1,932	
NNRTIs					
Efavirenz					
• Generic	600 mg tablet	30 tablets	\$894 to \$980	\$1,073 to \$1,117	\$768
• Sustiva	600 mg tablet	30 tablets	\$981	\$1,177	
Doravirine					
• Pifeltro	100 mg tablet	30 tablets	\$1,380	\$1,656	N/A
Etravirine					
• Intelence	200 mg tablet	60 tablets	\$1,366	\$1,628	N/A

Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) ^b	AWP (Monthly) ^b	FUL (As of Oct. 31, 2019) ^c
NNRTIs, continued					
Nevirapine					
• Generic	200 mg tablet	60 tablets	\$10 to \$45	\$648 to \$651	\$65
• Viramune	200 mg tablet	60 tablets	\$906	\$1,087	
• Generic XR	400 mg tablet	30 tablets	\$135 to \$565	\$595 to \$706	\$392
• Viramune XR	400 mg tablet	30 tablets	\$840	\$1,008	
Rilpivirine					
• Edurant	25 mg tablet	30 tablets	\$1,115	\$1,338	N/A
PIs					
Atazanavir					
• Generic	200 mg capsule	60 capsules	\$445 to \$1,264	\$1,517 to \$1,668	\$1,405
• Reyataz	200 mg capsule	60 capsules	\$1,463	\$1,756	
• Generic	300 mg capsule	30 capsules	\$445 to \$1,252	\$1,502 to \$1,652	\$1,032
• Reyataz	300 mg capsule	30 capsules	\$1,449	\$1,739	
Atazanavir/Cobicistat					
• Evotaz	300/150 mg tablet	30 tablets	\$1,605	\$1,927	N/A
Darunavir					
• Prezista	600 mg tablet	60 tablets	\$1,690	\$2,028	N/A
• Prezista	800 mg tablet	30 tablets	\$1,690	\$2,028	N/A
• Prezista	100 mg/mL suspension	200 mL	\$939	\$1,126	N/A
Darunavir/Cobicistat					
• Prezcoibix	800 mg/150 mg tablet	30 tablets	\$1,931	\$2,317	N/A
Lopinavir/Ritonavir					
• Kaletra	200 mg/50 mg tablet	120 tablets	\$1,024	\$1,229	N/A
Tipranavir					
• Aptivus	250 mg capsule	120 capsules	\$1,673	\$2,008	N/A
INSTIs					
Dolutegravir					
• Tivicay	50 mg tablet	30 tablets	\$1,740	\$2,089	N/A

Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) ^b	AWP (Monthly) ^b	FUL (As of Oct. 31, 2019) ^c
INSTIs, continued					
• Tivicay	50 mg tablet	60 tablets	\$3,480	\$4,178	N/A
Raltegravir					
• Isentress	400 mg tablet	60 tablets	\$1,574	\$1,889	N/A
• Isentress HD	600 mg tablet	60 tablets	\$1,574	\$1,889	N/A
Fusion Inhibitor					
Enfuvirtide					
• Fuzeon	90 mg injection kit	60 doses (1 kit)	\$3,586	\$4,303	N/A
CCR5 Antagonist					
Maraviroc					
• Selzentry	150 mg tablet	60 tablets	\$1,556	\$1,867	N/A
• Selzentry	300 mg tablet	60 tablets	\$1,556	\$1,867	N/A
• Selzentry	300 mg tablet	120 tablets	\$3,112	\$3,734	N/A
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk					
• Trogarzo	200 mg vial	8 vials	\$9,080	\$10,896	N/A
Coformulated Combination Products as Single-Tablet Regimens					
Bictegravir/Tenofovir Alafenamide/Emtricitabine					
• Biktarvy	50 mg/25 mg/200 mg tablet	30 tablets	\$3,089	\$3,707	N/A
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
• Symtuza	800 mg/150 mg/10 mg/200 mg tablet	30 tablets	\$3,722	\$4,466	N/A
Dolutegravir/Abacavir/Lamivudine					
• Triumeq	50 mg/600 mg/300 mg tablet	30 tablets	\$2,889	\$3,467	N/A
Dolutegravir/Lamivudine					
• Dovato	50 mg/300 mg tablet	30 tablets	\$2,295	\$2,754	N/A
Dolutegravir/Rilpivirine					
• Juluca	50 mg/25 mg tablet	30 tablets	\$2,707	\$3,249	N/A
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine					
• Delstrigo	100 mg/300 mg/300 mg tablet	30 tablets	\$2,100	\$2,520	N/A

Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) ^b	AWP (Monthly) ^b	FUL (As of Oct. 31, 2019) ^c
Coformulated Combination Products as Single-Tablet Regimens, continued					
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine					
• Atripla	600 mg/300 mg/200 mg tablet	30 tablets	\$2,858	\$3,429	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine					
• Symfi	600 mg/300 mg/150 mg tablet	30 tablets	\$1,634	\$1,961	N/A
• Symfi Lo	400 mg/300 mg/150 mg tablet	30 tablets	\$1,634	\$1,961	N/A
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
• Genvoya	150 mg/150 mg/10 mg/200 mg tablet	30 tablets	\$3,090	\$3,708	N/A
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine					
• Stribild	150 mg/150 mg/300 mg/200 mg tablet	30 tablets	\$3,241	\$3,889	N/A
Rilpivirine/Tenofovir Alafenamide/Emtricitabine					
• Odefsey	25 mg/25 mg/200 mg tablet	30 tablets	\$2,812	\$3,375	N/A
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine					
• Complera	25 mg/300 mg/200 mg tablet	30 tablets	\$2,812	\$3,375	N/A
PK Enhancers (Boosters)					
Cobicistat					
• Tybost	150 mg tablet	30 tablets	\$230	\$277	N/A
Ritonavir					
• Generic	100 mg tablet	30 tablets	\$80 to \$222	\$278	\$78
• Norvir	100 mg tablet	30 tablets	\$257	\$309	

^a The following less commonly used ARV drugs are not included in this table: DLV, ddI, FPV, IDV, NFV, SQV, and d4T.

^b Source: Micromedex Red Book [database]. IBM Watson Health. 2019. Available at: <https://www.micromedexsolutions.com>

^c Source: Federal Upper Limits—October 2019 [database]. Medicare & Medicaid Services. 2019. Available at: <https://www.medicare.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html>.

Key: ARV = antiretroviral; AWP = average wholesale price; CD4 = CD4 T lymphocyte; d4T = stavudine; ddI = didanosine; DLV = delavirdine; FPV = fosamprenavir; FUL = federal upper limit; HD = high dose; IDV = indinavir; INSTI = integrase strand transfer inhibitor; N/A = not applicable; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; SQV = saquinavir; WAC = wholesale acquisition cost; XR = extended release

Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

PK interactions may occur during absorption, metabolism, or elimination of the ARV drug and/or the interacting drug. This table does not include a comprehensive list of all possible mechanisms of interactions for individual ARV drugs (e.g., transporters); however, the table lists the most common mechanisms of known interactions and focuses on absorption and CYP- and UGT1A1-mediated interactions.

Note: N/A indicates that there are no clinically relevant interactions by the mechanism. Identified mechanisms are specific to the ARV drugs described in the row and may not be reflective of complete ARV regimens. The older PIs FPV, IDV, NFV, and SQV are not commonly used in clinical practice and are **not** included in this table. Please refer to the FDA product labels for FPV, IDV, NFV, and SQV for information regarding drug interactions with these PIs.

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
INSTIs							
BIC	N/A	Concentration decreased by products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)	Substrate	3A4	N/A	N/A	Substrate
DTG	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate
EVG/c	N/A		Inhibitor	3A4	3A4, 2D6	2C9	Substrate
RAL	N/A		N/A	N/A	N/A	N/A	Substrate
PIs							
ATV	Concentration decreased	N/A	Substrate, Inducer, Inhibitor	3A4	3A4, 2C8	N/A	Inhibitor
ATV/c	Concentration decreased	N/A	Substrate, Inhibitor	3A4	3A4, 2D6, 2C8	N/A	Inhibitor
ATV/r	Concentration decreased	N/A	Substrate, Inhibitor	3A4, 2D6	3A4, 2D6, 2C8	1A2, 2B6, 2C8, 2C9, 2C19	ATV: Inhibitor RTV: Inducer
DRV/c	N/A	N/A	Substrate, effect on P-gp unknown	3A4	3A4, 2D6	N/A	No data
DRV/r	N/A	N/A	Substrate, effect on P-gp unknown	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
LPV/r	N/A	N/A	Substrate	3A4, 2D6	3A4	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
TPV/r	N/A	N/A	Substrate, Inducer	3A4, 2D6	3A4, 2D6	No data	Inducer
NNRTIs							
DOR	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A
EFV	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A
ETR	N/A	N/A	N/A	3A4, 2C9, 2C19	2C9, 2C19	3A4	N/A

Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 2)

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
NNRTIs, continued							
NVP	N/A	N/A	N/A	3A4, 2B6	N/A	3A4, 2B6	N/A
RPV	Concentration decreased	N/A	N/A	3A4	N/A	N/A	N/A
NRTIs							
ABC	N/A	N/A	N/A	N/A	N/A	N/A	Substrate
FTC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3TC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
TAF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
TDF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
ZDV	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CCR5 Antagonist							
MVC	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
Fusion Inhibitor							
T-20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Post-Attachment Inhibitor							
IBA	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; **ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir**; BIC = bictegravir; Ca = calcium; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; **DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir**; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FPV = fosamprenavir; FTC = emtricitabine; **IBA = ibalizumab; IDV = indinavir**; INSTI = integrase strand transfer inhibitor; **LPV/r = lopinavir/ritonavir**; Mg = magnesium; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; **P-gp = P-glycoprotein**; PK = pharmacokinetic; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; **TPV/r = tipranavir/ritonavir**; UGT = uridine diphosphate glucuronosyltransferase; ZDV = zidovudine; Zn = zinc

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 19)

This table provides information on the known or predicted interactions between PIs and non-ARV drugs. When information is available, interactions for boosted ATV (with either RTV or COBI) and unboosted ATV are listed separately. The term “All PIs” refers to both unboosted ATV and PIs boosted with either RTV or COBI, except for FPV, IDV, NFV, and SQV. For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables [21c](#), [22a](#), and [22b](#).

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. **In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.**

Note: FPV, IDV, NFV, and SQV are no longer commonly used in clinical practice and are **not** included in this table. Please refer to the FDA product labels for FPV, IDV, NFV, and SQV for information regarding drug interactions between these PIs and concomitant medications.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV, ATV/c, ATV/r	When Given Simultaneously: • ↓ ATV expected	Administer ATV at least 2 hours before or 1–2 hours after antacids or buffered medications.
	TPV/r	TPV AUC ↓ 27%	Administer TPV at least 2 hours before or 1 hour after antacids.
H2 Receptor Antagonists	ATV (unboosted)	When Given Simultaneously with Famotidine: • ATV AUC ↓ 41% When Given 2 Hours Before and ≥10 Hours After H2RA: • ↔ ATV	A single dose of H2RA should not exceed a dose equivalent to famotidine 20 mg, and the total daily dose should not exceed a dose equivalent to famotidine 20 mg twice daily in PI-naïve patients. Give ATV at least 2 hours before and at least 10 hours after the H2RA. Do not coadminister unboosted ATV plus H2RA in PI-experienced patients.
	ATV/c, ATV/r	↓ ATV expected	H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naïve patients or famotidine 20 mg twice daily in ART-experienced patients. Give ATV 300 mg (plus COBI 150 mg or RTV 100 mg) simultaneously with and/or ≥10 hours after the dose of H2RA. If using TDF and H2RA in ART-experienced patients, use ATV 400 mg (plus COBI 150 mg or RTV 100 mg).
	DRV/c, DRV/r, LPV/r, TPV/r	With Ranitidine: • ↔ DRV/r ↔ PI expected	No dose adjustment needed.
Proton Pump Inhibitors	ATV (unboosted)	With Omeprazole 40 mg: • ATV AUC ↓ 94%	Do not coadminister.
	ATV/c, ATV/r	With Omeprazole 40 mg: • ATV AUC ↓ 76% When Omeprazole 20 mg is Given 12 Hours before ATV/c or ATV/r: • ATV AUC ↓ 42%	PPI dose should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naïve patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. Do not coadminister in PI-experienced patients.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers, continued			
Proton Pump Inhibitors	DRV/c, LPV/r	↔ PI expected	No dose adjustment needed.
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole efficacy. If patient does not experience symptomatic relief, increase dose to no more than omeprazole 40 mg daily.
	TPV/r	↔ TPV/r Omeprazole AUC ↓ 70%	Do not coadminister.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	All PIs	↑ alfuzosin expected	Contraindicated.
Doxazosin	All PIs	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate while monitoring for clinical response/adverse events. Dose reduction may be necessary.
Tamsulosin	All PIs	↑ tamsulosin expected	Do not coadminister, unless benefits outweigh risks. If coadministered, monitor for tamsulosin toxicities.
Terazosin	All PIs	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate while monitoring for clinical response/adverse events. Dose reduction may be necessary.
Silodosin	All PIs	↑ silodosin expected	Contraindicated.
Antibacterials			
Antimycobacterials			
Bedaquiline	All PIs	With LPV/r: • Bedaquiline AUC ↑ 1.9-fold With other PI/r, ATV/c, or DRV/c: • ↑ bedaquiline possible	Do not coadminister, unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	ATV (unboosted)	↑ rifabutin AUC expected	Recommended dose is rifabutin 150 mg once daily. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	ATV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus ATV/r: • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	
	DRV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) plus DRV/r: • ↔ rifabutin AUC and metabolite AUC ↑ 881%	
	LPV/r	Compared with Rifabutin (300 mg Daily) Alone, Rifabutin (150 mg Once Daily) plus LPV/r: • Rifabutin AUC ↑ 203% and metabolite AUC ↑ 375%	
	TPV/r	Rifabutin AUC ↑ 190% and metabolite AUC ↑ 1,971%	
	PI/c	↑ rifabutin expected ↓ COBI expected	Do not coadminister.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials, continued			
Antimycobacterials, continued			
Rifampin	All PIs	↓ PI concentration by >75%	Contraindicated. Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose is not recommended. Consider rifabutin if a rifamycin is indicated.
Rifapentine	All PIs	↓ PI expected	Do not coadminister.
Macrolides			
Azithromycin	ATV (unboosted), ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed.
	DRV/c, DRV/r, TPV/r	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	ATV (unboosted)	Clarithromycin AUC ↑ 94%	Reduce clarithromycin dose by 50% or consider alternative ARV or azithromycin. Monitor for clarithromycin-related adverse events, including QTc prolongation.
	PI/c, PI/r	DRV/r ↑ clarithromycin AUC 57% LPV/r ↑ clarithromycin expected RTV 500 mg twice daily ↑ clarithromycin 77% TPV/r ↑ clarithromycin 19% Clarithromycin ↑ TPV 66%	Consider alternative ARV or azithromycin. Monitor for clarithromycin-related adverse events, including QTc prolongation. If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl <30 mL/min, reduce clarithromycin dose by 75%.
Erythromycin	All PIs	↑ erythromycin expected ↑ PIs expected	Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	PI/c, PI/r	↑ apixaban expected	Do not coadminister in patients who require apixaban 2.5 mg twice daily. In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily: • Reduce apixaban dose by 50%.
Betrixaban	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	ATV/c, ATV/r, LPV/r	↑ betrixaban expected	Administer an initial single dose of betrixaban 80 mg followed by betrixaban 40 mg once daily.
	DRV/c, DRV/r, TPV/r	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
Dabigatran	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	ATV/c, ATV/r, LPV/r	↑ dabigatran expected With COBI 150 mg Alone: • Dabigatran AUC ↑ 110% to 127%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.
	DRV/c, DRV/r, TPV/r	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants, continued			
Edoxaban	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	ATV/c, ATV/r, LPV/r	↑ edoxaban expected	Stroke Prevention in Nonvalvular Atrial Fibrillation Indication: • No dose adjustment needed. Deep Venous Thrombosis and Pulmonary Embolism Indication: • Administer edoxaban 30 mg once daily.
	DRV/c, DRV/r, TPV/r	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
Rivaroxaban	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	PI/c, PI/r	↑ rivaroxaban expected	Do not coadminister.
Warfarin	PI/c	No data	Monitor INR closely when stopping or starting PI/c or PI/r and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	PI/r	↓ warfarin possible	
Anticonvulsants			
Carbamazepine	ATV (unboosted)	May ↓ PI concentrations substantially	Do not coadminister.
	ATV/r, LPV/r, TPV/r	↑ carbamazepine possible TPV/r ↑ carbamazepine AUC 26% May ↓ PI concentrations substantially	Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response. Do not coadminister with LPV/r once daily.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	PI/c	↑ carbamazepine possible ↓ cobicistat expected ↓ PI expected	Contraindicated.
Eslicarbazepine	All PIs	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	All PIs	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	ATV (unboosted)	↔ lamotrigine	No dose adjustment needed.
	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant.
	LPV/r	Lamotrigine AUC ↓ 50% ↔ LPV	
	DRV/r, TPV/r	↓ lamotrigine possible	
	PI/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants, continued			
Oxcarbazepine	All PIs	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	ATV (unboosted)	↓ ATV expected	Do not coadminister.
	ATV/r, DRV/r, TPV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	LPV/r	↓ phenytoin possible ↓ LPV/r possible	Do not coadminister with LPV/r once daily. Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	PI/c	↓ cobicistat expected ↓ PI expected	Contraindicated.
Phenytoin	ATV (unboosted)	↓ ATV expected	Do not coadminister.
	ATV/r, DRV/r, TPV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	LPV/r	Phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Do not coadminister with LPV/r once daily. Consider alternative anticonvulsant or monitor concentrations of both drugs and assess virologic response.
	PI/c	↓ cobicistat expected ↓ PI expected	Contraindicated.
Valproic Acid	All PIs	↓ or ↔ VPA possible LPV AUC ↑ 38% No data for other PIs	Monitor VPA concentrations and monitor for PI tolerability.
Antidepressants, Anxiolytics, and Antipsychotics			
Also see Sedative/Hypnotics section below			
Bupropion	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	TPV/r	Bupropion AUC ↓ 46%	
	LPV/r	Bupropion AUC ↓ 57%	
	PI/c	↔ bupropion expected	No dose adjustment needed.
Buspirone	All PIs	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response.
Nefazodone	All PIs	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and PI tolerability.
Trazodone	All PIs	RTV 200 mg twice daily (for 2 days) ↑ trazodone AUC 240%	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 6 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics, continued			
Also see Sedative/Hypnotics section below			
Tricyclic Antidepressants Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine	All PIs	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	All PIs except DRV/r	No data	Titrate SSRI dose using the lowest available initial or maintenance dose.
Antipsychotics			
Aripiprazole	PI/c, PI/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ aripiprazole expected	Administer 50% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Brexipiprazole	PI/c, PI/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ brexpiprazole expected	Administer 50% of the usual brexpiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Cariprazine	All PIs	↑ cariprazine expected	<p>Starting Cariprazine in a Patient Who Is Already Receiving a PI:</p> <ul style="list-style-type: none"> Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. <p>Starting a PI in a Patient Who Is Already Receiving Cariprazine:</p> <ul style="list-style-type: none"> For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, cariprazine dose may need to be increased.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 7 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics, continued			
Also see Sedative/Hypnotics section below			
Antipsychotics, continued			
Iloperidone	All PIs	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lurasidone	ATV (unboosted)	↑ lurasidone expected	Consider alternative ARV or antipsychotic. If coadministration is necessary, reduce lurasidone dose by 50%.
	PI/c, PI/r	↑ lurasidone expected	Contraindicated.
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., clozapine, perphenazine, risperidone, thioridazine)	PI/c, PI/r	↑ antipsychotic possible	Titrate antipsychotic dose using the lowest initial dose or adjust maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.
Pimavanserin	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or antipsychotic.
	LPV/r	↑ pimavanserin expected	Do not coadminister , due to risk for QTc prolongation.
	All other PIs	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	All PIs	↑ pimozide expected	Contraindicated.
Quetiapine	All PIs	↑ quetiapine expected	Starting Quetiapine in a Patient Receiving a PI: • Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events.
			Starting a PI in a Patient Receiving a Stable Dose of Quetiapine: • Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events.
Ziprasidone	LPV/r	↑ ziprasidone expected	Do not coadminister , due to risk for QTc prolongation.
	All PIs except LPV/r	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events.
Antifungals			
Fluconazole	TPV/r	TPV AUC ↑ 50%	Fluconazole doses >200 mg daily are not recommended . If high-dose fluconazole is indicated, consider alternative ARV.
	All PIs except TPV/r	↔ PI expected ↔ fluconazole expected	No dose adjustment needed.
Isavuconazole	LPV/r	Isavuconazole AUC ↑ 96% LPV AUC ↓ 27% RTV AUC ↓ 31%	If coadministered, monitor isavuconazole concentrations and adverse events. Monitor for virologic response.
	All PIs except LPV/r	↑ isavuconazole possible ↑ or ↓ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability and virologic response.
Itraconazole	All PIs	↑ itraconazole possible ↑ PI possible	Itraconazole doses >200 mg/day are not recommended with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole concentrations.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 8 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Posaconazole	ATV	ATV AUC ↑ 268% ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations and monitor for posaconazole-related or PI-related adverse events.
	ATV/r	ATV AUC ↑ 146% ↑ posaconazole possible	
	All other PIs	↑ PI possible ↑ posaconazole possible	
Voriconazole	ATV (unboosted)	↑ PI possible ↑ voriconazole possible	If coadministered, monitor voriconazole concentrations and monitor for voriconazole-related or PI-related adverse events.
	PI/c	No data	Do not coadminister voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	PI/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			
Artemether/Lumefantrine	ATV (unboosted), PI/c	↑ lumefantrine expected No data for artemether	Clinical significance unknown. If coadministered, monitor closely for antimalarial efficacy and lumefantrine toxicity, including QTc prolongation.
	DRV/r	Artemether AUC ↓ 16% DHA ^a AUC ↓ 18% Lumefantrine AUC ↑ 175% ↔ DRV	
	LPV/r	Artemether AUC ↓ 40% DHA AUC ↓ 45% Lumefantrine AUC ↑ 4.8-fold ↔ LPV	
	TPV/r	↑ lumefantrine expected	Do not coadminister, due to risk for QTc prolongation.
Atovaquone/Proguanil	ATV/r, LPV/r	With ATV/r: • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% With LPV/r: • Atovaquone AUC ↓ 74% • Proguanil AUC ↓ 38%	Clinical significance unknown. Consider alternative ARV or malaria prophylaxis.
Mefloquine	All PIs	With RTV 200 mg Twice Daily: • RTV AUC ↓ 31% and C _{min} ↓ 43% • ↔ mefloquine With ATV (unboosted), PI/c, or PI/r: • No data • ↑ mefloquine possible	Clinical significance unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 9 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiplatelets			
Clopidogrel	All PIs	Clopidogrel active metabolite AUC ↓ 320% with impaired platelet inhibition	Do not coadminister.
Prasugrel	All PIs	Prasugrel active metabolite AUC ↓ 210% with adequate platelet inhibition	Insufficient data to make a recommendation.
Ticagrelor	All PIs	↑ ticagrelor expected	Do not coadminister.
Vorapaxar	All PIs	↑ vorapaxar expected	Do not coadminister.
Antipneumocystis and Antitoxoplasmosis Drug			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed.
	All other PIs	↔ atovaquone expected	No dose adjustment needed.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV (unboosted), ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed.
	DRV/c, DRV/r, LPV/r, TPV/r	↔ arformoterol expected	No dose adjustment needed.
Indacaterol	All PIs	With RTV 300 mg Twice Daily: • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	All PIs	↑ olodaterol expected	No dose adjustment needed.
Salmeterol	All PIs	↑ salmeterol possible	Do not coadminister , due to potential increased risk of salmeterol-associated CV events.
Cardiac Medications			
Amiodarone	TPV/r	↑ amiodarone possible ↑ PI possible	Contraindicated.
	All other PIs	↑ amiodarone possible ↑ PI possible	Do not coadminister unless benefits outweigh risks. If coadministered , monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.
Antiarrhythmics (e.g., disopyramide, dofetilide, lidocaine, mexiletine, propafenone)	ATV (unboosted)	↑ antiarrhythmic possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic toxicities.
	PI/c, PI/r	↑ antiarrhythmic possible	Do not coadminister.
Dronedarone	ATV (unboosted)	↑ dronedarone possible	Do not coadminister.
	PI/c, PI/r	↑ dronedarone expected	Contraindicated.
Flecainide	All PIs except TPV/r	↑ flecainide possible	Do not coadminister.
	TPV/r	↑ flecainide expected	Contraindicated.
Propafenone	All PIs except TPV/r	↑ propafenone possible	Do not coadminister.
	TPV/r	↑ propafenone expected	Contraindicated.
Quinidine	All PIs except TPV/r	↑ quinidine possible	Do not coadminister.
	TPV/r	↑ quinidine expected	Contraindicated.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications, continued			
Beta-Blockers (e.g., carvedilol, metoprolol, timolol)	All PIs	↑ beta-blockers possible	May need to decrease beta-blocker dose; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
Bosentan	All PIs	With LPV/r: • ↑ bosentan 48-fold (Day 4) and ↑ 5-fold (Day 10) ↓ ATV expected	Do not coadminister bosentan and unboosted ATV. In Patients on a PI (Other than Unboosted ATV) >10 Days: • Start bosentan at 62.5 mg once daily or every other day. In Patients on Bosentan who Require a PI (Other than Unboosted ATV): • Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day. When Switching Between COBI and RTV: • Maintain same bosentan dose.
Calcium Channel Blockers, Except Diltiazem	All PIs	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.
Digoxin	PI/c, PI/r	RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C _{max} 41% and ↔ AUC	Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Diltiazem	ATV (unboosted), ATV/c, ATV/r	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ likely with ATV/c or ATV/r	Decrease diltiazem dose by 50%. ECG monitoring is recommended.
	DRV/c, DRV/r, LPV/r, TPV/r	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and toxicities.
Eplerenone	PI/c, PI/r	↑ eplerenone expected	Contraindicated.
Ranolazine	ATV (unboosted)	↑ ranolazine possible	Do not coadminister.
	PI/c, PI/r	↑ ranolazine expected	Contraindicated.
Ivabradine	All PIs	↑ ivabradine expected	Contraindicated.
Corticosteroids			
Beclomethasone Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold	No dose adjustment needed.
	All PIs except DRV/r	↔ 17-BMP expected	No dose adjustment needed.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 11 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids, continued			
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	All PIs	↑ glucocorticoids possible RTV 100 mg twice daily ↑ fluticasone AUC 350-fold	Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	All PIs	↑ glucocorticoids possible ↓ PI possible	Do not coadminister unless potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	All PIs	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	LPV/r	↑ prednisolone AUC 31%	Coadministration may be considered if the potential benefits outweigh the risks of adverse events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-associated toxicities.
	All PIs	↑ prednisolone possible	
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	All PIs	↑ glucocorticoids expected	Do not coadminister. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Glucose-Lowering Medications			
Canagliflozin	ATV (unboosted), PI/c	↔ canagliflozin	No dose adjustment needed.
	PI/r	↓ canagliflozin expected	<p>If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily.</p> <p>If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function.</p> <p>In Patients with eGFR ≥60 mL/min/1.73 m²:</p> <ul style="list-style-type: none"> • Canagliflozin dose may be increased to 300 mg daily. <p>In Patients with eGFR <60 mL/min/1.73 m²:</p> <ul style="list-style-type: none"> • Consider adding another antihyperglycemic agent.
Saxagliptin	All PIs	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	All PIs	↑ saxagliptin expected	Do not coadminister. Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination is not recommended .

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 12 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	ATV/c, ATV/r	↑ daclatasvir	Decrease daclatasvir dose to 30 mg once daily.
	ATV (unboosted), DRV/c, DRV/r, LPV/r	↔ daclatasvir	No dose adjustment needed.
	TPV/r	No data	No data available for dose recommendation.
Dasabuvir plus Paritaprevir/Ombitasvir/RTV	ATV (unboosted)	↔ ATV	ATV 300 mg alone, without COBI or additional RTV , should be given in the morning with dasabuvir plus paritaprevir/ombitasvir/RTV.
	ATV/c, ATV/r	No data	This HCV regimen contains RTV. If ATV is part of the ARV regimen, prescribe ATV 300 mg daily without COBI or RTV. ATV should be administered in the morning, at the same time as ombitasvir/paritaprevir/RTV plus dasabuvir. Resume RTV or COBI regimen when HCV therapy is completed.
	DRV	DRV C _{min} ↓ 43% to 48%	Do not coadminister.
	LPV/r	Paritaprevir AUC ↑ 117%	Do not coadminister.
	DRV/c, TPV/r	No data	Do not coadminister.
Elbasvir/Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold Elbasvir ↔ ATV Grazoprevir ↑ ATV AUC 43%	Contraindicated. May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.
	DRV/r	Elbasvir AUC ↑ 66% Grazoprevir AUC ↑ 7.5-fold ↔ DRV	
	LPV/r	Elbasvir AUC ↑ 3.7-fold Grazoprevir AUC ↑ 12.9-fold ↔ LPV	
	ATV (unboosted), ATV/c, DRV/c, TPV/r	↑ grazoprevir expected	

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 13 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Glecaprevir/Pibrentasvir	ATV (unboosted), ATV/c, ATV/r	With (ATV 300 mg plus RTV 100 mg) Once Daily: • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	Contraindicated.
	DRV/c, DRV/r	With (DRV 800 mg plus RTV 100 mg) Once Daily: • Glecaprevir AUC ↑ 5-fold • ↔ pibrentasvir	Do not coadminister.
	LPV/r	Glecaprevir AUC ↑ 4-fold Pibrentasvir ↑ 2.5-fold	Do not coadminister.
	TPV/r	↑ glecaprevir and pibrentasvir expected	Do not coadminister.
Ledipasvir/Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment needed. Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased risk of TDF toxicities. If coadministration is necessary, monitor for TDF-associated adverse reactions.
	ATV (unboosted), ATV/c, DRV/c, DRV/r, LPV/r	↔ PI expected ↔ ledipasvir and sofosbuvir	
	TPV/r	↓ ledipasvir and sofosbuvir expected	Do not coadminister.
Sofosbuvir	TPV/r	↓ sofosbuvir expected	Do not coadminister.
Sofosbuvir/Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment needed.
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment needed.
	ATV (unboosted), ATV/c, DRV/c, LPV/r	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed.
	TPV/r	↓ sofosbuvir expected ↓ velpatasvir expected	Do not coadminister.
Sofosbuvir/Velpatasvir/Voxilaprevir	ATV (unboosted), ATV/c, ATV/r	With ATV/r: • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	Do not coadminister.
	LPV/r	↑ voxilaprevir expected	Do not coadminister.
	DRV/c, DRV/r	With DRV/r: • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 14 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Sofosbuvir/Velpatasvir/Voxilaprevir, continued	TPV/r	↓ sofosbuvir expected ↓ velpatasvir expected Effect on voxilaprevir is unknown.	Do not coadminister.
Herbal Products			
St. John's Wort	All PIs	↓ PI expected	Contraindicated.
Hormonal Therapies			
Contraceptives – Injectable Depot MPA	LPV/r	MPA AUC ↑ 46% and ↔ C _{min}	No dose adjustment needed.
	All other PIs	No data	No dose adjustment needed.
Contraceptives – Oral	ATV (unboosted)	Ethinyl estradiol AUC ↑ 48% Norethindrone AUC ↑ 110%	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol ^b or use alternative ARV or contraceptive methods. Oral contraceptives that contain less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.
	ATV/c	Drospirenone AUC ↑ 2.3-fold Ethinyl estradiol AUC ↓ 22%	Contraindicated with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or contraceptive methods.
		↔ ethinyl estradiol AUC and C _{min} ↓ 25% ↔ levonorgestrel	No dose adjustment needed.
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C _{min} ↓ 37% Norgestimate AUC ↑ 85% Norethindrone AUC ↑ 51% and C _{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol. ^c Oral contraceptives that contain progestins other than norethindrone or norgestimate have not been studied.
	DRV/c	Drospirenone AUC ↑ 1.6-fold Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/r, LPV/r, TPV/r	Ethinyl estradiol AUC ↓ 37% to 55% Norethindrone AUC ↓ 14% to 34% With TPV/r: • ↔ norethindrone AUC	When Used for Contraception: • Use alternative ARV or contraceptive methods. When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation): • Monitor for clinical effectiveness of hormonal therapy.
Contraceptives – Subdermal Implant Etonogestrel	LPV/r	Etonogestrel AUC ↑ 52% and C _{min} ↑ 34%	No dose adjustment needed.
	All other PIs	No data	
Contraceptives – Transdermal Ethinyl Estradiol/ Norelgestromin	LPV/r	↔ LPV Ethinyl estradiol AUC ↓ 45% Norelgestromin AUC ↑ 83%	No dose adjustment needed.
	All other PIs	No data	
Contraceptives – Vaginal Ring Etonogestrel/Ethinyl Estradiol	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed.
	All other PIs	No data	

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 15 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Contraceptives – Vaginal Ring Segesterone/Ethinyl Estradiol	All PIs	No data	Use alternative ARV or contraceptive methods.
Gender-Affirming Therapy	PI/c	↓ or ↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects and endogenous hormone concentrations.
	PI/r	↓ estradiol possible	
	All PIs	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed.
	All PIs	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations. No dose adjustment needed for finasteride.
	All PIs	↓ testosterone possible	Adjust testosterone dose as needed based on clinical effects and endogenous hormone concentrations.
Menopausal Replacement Therapy	All PIs	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	All PIs	↑ drospirenone possible ↑ medroxyprogesterone ↑ micronized progesterone See Hormonal Contraceptives for other progestin-PI interactions	Adjust progestin/progesterone dose as needed based on clinical effects. Because drospirenone is prescribed at a lower dose for menopausal HRT than the products used for hormonal contraceptives, it is not contraindicated with ATV/c products.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	All PIs	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Lipid-Modifying Agents			
Atorvastatin	ATV (unboosted), ATV/r	↑ atorvastatin possible	Titrate atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold and C _{max} ↑ 18.9-fold	Do not coadminister.
	DRV/c	Atorvastatin AUC ↑ 3.9-fold and C _{max} ↑ 4.2-fold	Titrate atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Titrate atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	LPV/r	Atorvastatin AUC ↑ 5.9-fold and C _{max} ↑ 4.7-fold	Titrate atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	TPV/r	Atorvastatin AUC ↑ 9.4-fold and C _{max} ↑ 8.6-fold	Do not coadminister.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 16 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying Agents, continued			
Lomitapide	All PIs except TPV/r	↑ lomitapide expected	Contraindicated.
	TPV/r	↑ lomitapide expected	Titrate lomitapide dose based on clinical response. Do not exceed lomitapide 30 mg daily.
Lovastatin	All PIs	Significant ↑ lovastatin expected	Contraindicated.
Pitavastatin	All PIs	ATV ↑ pitavastatin AUC 31% and C _{max} ↑ 60% ↔ ATV DRV/r ↓ pitavastatin AUC 26% ↔ DRV/r LPV/r ↓ pitavastatin AUC 20% ↔ LPV	No dose adjustment needed.
Pravastatin	ATV/c, ATV/r	No data	Titrate pravastatin dose carefully while monitoring for pravastatin-related adverse events.
	DRV/c, DRV/r	With DRV/r: • Pravastatin AUC ↑ 81% following single dose of pravastatin Pravastatin AUC ↑ 23% at steady state	Titrate pravastatin dose carefully while monitoring for pravastatin-related adverse events.
	LPV/r	Pravastatin AUC ↑ 33%	No dose adjustment needed.
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold and C _{max} ↑ 7-fold	Titrate rosuvastatin dose carefully and administer lowest effective dose while monitoring for rosuvastatin-related adverse events. Do not exceed rosuvastatin 10 mg daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold and C _{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold and C _{max} ↑ 3.8-fold	Titrate rosuvastatin dose carefully and administer lowest effective dose while monitoring for rosuvastatin-related adverse events. Do not exceed rosuvastatin 20 mg daily.
	DRV/r	Rosuvastatin AUC ↑ 48% and C _{max} ↑ 2.4-fold	Titrate rosuvastatin dose carefully and administer the lowest effective dose while monitoring for rosuvastatin-related adverse events.
	LPV/r	Rosuvastatin AUC ↑ 2.1-fold and C _{max} ↑ 4.7-fold	Titrate rosuvastatin dose carefully and administer the lowest effective dose. Do not exceed rosuvastatin 10 mg daily.
	TPV/r	Rosuvastatin AUC ↑ 26% and C _{max} ↑ 2.2-fold	No dose adjustment needed.
Simvastatin	All PIs	Significant ↑ simvastatin expected	Contraindicated.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV (unboosted)	Buprenorphine AUC ↑ 93% Norbuprenorphine (active metabolite) AUC ↑ 76% ↓ ATV possible	Do not coadminister.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 17 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence, continued			
Buprenorphine Sublingual, buccal, or implant, continued	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%	Monitor for sedation and other signs or symptoms of over-medication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments.
	DRV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C _{min} ↑ 71%	No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	LPV/r	↔ LPV/r	
	TPV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC, C _{max} , and C _{min} ↓ 80% TPV C _{min} ↓ 19% to 40%	Consider monitoring TPV concentration. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	PI/c	No data	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Monitor for buprenorphine-related adverse events.
Fentanyl	All PIs	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV (unboosted)	↔ lofexidine expected	No dose adjustment needed.
	PI/c, PI/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV (unboosted)	↔ ATV	No dose adjustment needed.
	PI/c	No data	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.
	All PI/r	ATV/r and DRV/r ↓ R-methadone ^d AUC 16% to 18% LPV/r ↓ methadone AUC 26% to 53% TPV/r ↓ R-methadone ^d AUC 48%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.
Oxycodone	All PIs	LPV/r ↑ oxycodone AUC 2.6-fold Other PIs: ↑ oxycodone expected	Monitor for opioid-related adverse events. Oxycodone dose reduction may be necessary.
Tramadol	All PIs	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	ATV (unboosted)	No data	Avanafil dose should not exceed 50 mg once every 24 hours.
	PI/c, PI/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C _{max} 2.4-fold	Do not coadminister.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 18 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors, continued			
Sildenafil	All PIs	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg twice daily ↑ sildenafil AUC 1,000%	For Treatment of Erectile Dysfunction: • Start with sildenafil 25 mg every 48 hours and monitor for adverse events of sildenafil. Contraindicated for treatment of PAH.
Tadalafil	All PIs	RTV 200 mg twice daily ↑ tadalafil AUC 124% TPV/r (first dose) ↑ tadalafil AUC 133%	For Treatment of Erectile Dysfunction: • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse events of tadalafil. For Treatment of PAH <i>In Patients on a PI >7 Days:</i> • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. <i>In Patients on Tadalafil who Require a PI:</i> • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. <i>In Patients Switching between COBI and RTV:</i> • Maintain tadalafil dose. For Treatment of Benign Prostatic Hyperplasia: • Maximum recommended daily dose is tadalafil 2.5 mg per day.
Vardenafil	All PIs	RTV 600 mg twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse events of vardenafil.
Sedative/Hypnotics			
Alprazolam, Clonazepam, Diazepam	All PIs	↑ benzodiazepine possible RTV 200 mg twice daily (for 2 days) ↑ alprazolam half-life 222% and ↑ AUC 248%	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
Lorazepam, Oxazepam, Temazepam	All PIs	No data	These benzodiazepines are metabolized via non-CYP450 pathways; thus, there is less interaction potential than with other benzodiazepines.
Midazolam	All PIs	↑ midazolam expected	Oral midazolam is contraindicated with PIs. Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation.
Suvorexant	All PIs	↑ suvorexant expected	Do not coadminister.
Triazolam	All PIs	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	Contraindicated.
Zolpidem	PI/c, PI/r	↑ zolpidem possible	Initiate zolpidem at a low dose. Dose reduction may be necessary.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 19 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Drugs			
Calcifediol	All PIs	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.
Cisapride	All PIs	↑ cisapride expected	Contraindicated.
Colchicine	All PIs	RTV 100 mg twice daily ↑ colchicine AUC 296% and C _{max} ↑ 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	For Treatment of Gout Flares: • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For Prophylaxis of Gout Flares: • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. For Treatment of Familial Mediterranean Fever: • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg twice daily. Do not coadminister in patients with hepatic or renal impairment.
Dronabinol	All PIs	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	All PIs	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Ergot Derivatives	All PIs	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Contraindicated.
Flibanserin	All PIs	↑ flibanserin expected	Contraindicated.

^a DHA is an active metabolite of artemether.

^b The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations may also be available.

^c The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Brevicon; Femcon Fe; Modicon; Norinyl 1/35; Ortho-Cyclen; Ortho-Novum 1/35, 7/7/7; Ortho Tri-Cyclen; Ovcon 35; Tri-Norinyl. Generic formulations may also be available.

^d R-methadone is the active form of methadone.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; FDA = Food and Drug Administration; FPV = fosamprenavir; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; IDV = indinavir; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; NFV = nelfinavir; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = Phosphodiesterase Type 5; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV = ritonavir; SQV = saquinavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; VPA = valproic acid

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Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 12)

This table provides information on the known or predicted interactions between NNRTIs and non-ARV drugs. For information regarding interactions between NNRTIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. **In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.**

Note: DLV is **not** included in this table. Please refer to the FDA product label for information regarding drug interactions between DLV and other concomitant drugs. The term “All NNRTIs” in this table refers to all NNRTIs **except** for DLV.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV, NVP	↔ NNRTI AUC	No dose adjustment needed.
	ETR	↔ ETR expected	No dose adjustment needed.
	RPV	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR, ETR, NVP	↔ NNRTI expected	No dose adjustment needed.
	EFV	↔ EFV AUC	No dose adjustment needed.
	RPV	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
PPIs	DOR	DOR AUC ↓ 17% and C _{min} ↓ 16%	No dose adjustment needed.
	EFV, NVP	↔ EFV and NVP expected	
	ETR	↔ ETR AUC	
	RPV	With Omeprazole 20 mg Daily: • RPV AUC ↓ 40% and C _{min} ↓ 33%	Contraindicated.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin, Doxazosin, Silodosin	DOR, RPV	↔ alpha-adrenergic antagonists expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV	↔ tamsulosin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4 mg dose.
Antibacterials			
Antimycobacterials			
Bedaquiline	DOR, RPV	↔ bedaquiline expected	No dose adjustment needed.
	EFV, ETR	↓ bedaquiline possible	Do not coadminister.
	NVP	↔ bedaquiline AUC	No dose adjustment needed.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials, continued			
Antimycobacterials, continued			
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment needed for rifabutin.
	EFV	Rifabutin ↓ 38%	The recommended dosing range is rifabutin 450–600 mg per day.
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	Do not coadminister ETR plus PI/r with rifabutin. Use rifabutin 300 mg once daily if ETR is administered without PI/r.
	NVP	Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C _{min} ↓ 16%	No dose adjustment needed.
	RPV	Rifabutin plus RPV 50 mg Once Daily Compared to RPV 25 mg Once Daily Alone: • ↔ RPV AUC and C _{min}	Increase RPV dose to 50 mg once daily. No dose adjustment for rifabutin needed.
Rifampin	DOR	DOR AUC ↓ 88%	Contraindicated.
	EFV	EFV AUC ↓ 26%	Do not use EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	Do not coadminister.
	NVP	NVP ↓ 20% to 58%	Do not coadminister.
	RPV	RPV AUC ↓ 80%	Contraindicated.
Rifapentine	DOR, RPV	↓ NNRTI expected	Contraindicated.
	EFV	↔ EFV concentrations	No dose adjustment needed.
	ETR, NVP	↓ NNRTI possible	Do not coadminister.
Macrolides			
Azithromycin	All NNRTIs	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	DOR, RPV	↔ clarithromycin expected ↑ DOR and RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	NVP	Clarithromycin AUC ↓ 31% NVP AUC ↑ 26%	Monitor for effectiveness or consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
Erythromycin	DOR, RPV	↑ DOR and RPV possible	Monitor for ARV tolerability if used in combination.
	EFV, ETR, NVP	↑ EFV, ETR, and NVP possible ↓ erythromycin possible	Monitor for antibiotic efficacy if used in combination.
Anticoagulants			
Apixaban	DOR, RPV	↔ apixaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants, continued			
Betrixaban	All NNRTIs	↔ betrixaban expected	No dose adjustment needed.
Dabigatran	All NNRTIs	↔ dabigatran expected	No dose adjustment needed.
Edoxaban	All NNRTIs	↔ edoxaban expected	No dose adjustment needed.
Rivaroxaban	DOR, RPV	↔ rivaroxaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV	↔ warfarin expected	No dose adjustment needed.
	EFV, ETR, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine, Phenobarbital, Phenytoin	DOR, RPV	↓ NNRTI possible	Contraindicated.
	EFV	Carbamazepine plus EFV: • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% Phenytoin plus EFV: • ↓ EFV • ↑ or ↓ phenytoin possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and EFV concentrations.
	ETR	↓ anticonvulsant and ETR possible	Do not coadminister.
	NVP	↓ anticonvulsant and NVP possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and NVP concentrations and virologic response.
Eslicarbazepine	All NNRTIs	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV	↓ NNRTI possible	Contraindicated.
	EFV, ETR, NVP	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV	↔ anticonvulsant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ anticonvulsant possible	Monitor seizure control and consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, NVP, RPV	↔ lamotrigine expected	No dose adjustment needed.
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antidepressants, Anxiolytics, and Antipsychotics			
Antidepressants			
Bupropion	DOR, ETR, RPV	↔ bupropion expected	No dose adjustment needed.
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
	NVP	↓ bupropion possible	

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics, continued			
<i>Antidepressants, continued</i>			
Citalopram, Escitalopram	DOR, RPV	↔ antidepressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Fluoxetine, Fluvoxamine	All NNRTIs	↔ antidepressant expected	No dose adjustment needed.
Paroxetine	DOR, NVP, RPV	↔ paroxetine expected	No dose adjustment needed.
	EFV, ETR	↔ paroxetine expected	No dose adjustment needed.
Nefazodone	DOR, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect and titrate dose as necessary based on clinical response.
Sertraline	DOR, RPV	↔ sertraline expected	No dose adjustment needed.
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect and titrate dose as necessary based on clinical response.
	ETR, NVP	↓ sertraline possible	
Trazodone	DOR, RPV	↔ trazodone expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
<i>Anxiolytics (Benzodiazepines)</i>			
Alprazolam, Triazolam	DOR, RPV	↔ benzodiazepine expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ benzodiazepine possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV	↔ diazepam expected	No dose adjustment needed.
	EFV, NVP	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	DOR, ETR, NVP, RPV	↔ lorazepam expected	No dose adjustment needed.
	EFV	↔ lorazepam AUC	No dose adjustment needed.
Midazolam	DOR, RPV	↔ midazolam expected	No dose adjustment needed.
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C _{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	NVP	↓ midazolam possible	Monitor for therapeutic effectiveness of midazolam.
<i>Antipsychotics</i>			
Aripiprazole	DOR, RPV	↔ aripiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antipsychotics , continued			
Brexpiprazole	DOR, RPV	↔ brexpiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV	↔ cariprazine expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ cariprazine and ↑ or ↓ active metabolite possible	Do not coadminister.
Lurasidone	DOR, RPV	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine	DOR, ETR, NVP, RPV	↔ olanzapine expected	No dose adjustment needed.
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Pimavanserin	DOR, RPV	↔ pimavanserin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimavanserin expected	Do not coadminister.
Pimozide	DOR, RPV	↔ pimozide expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Antifungals			
Fluconazole	DOR, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV	↔ fluconazole expected ↔ EFV AUC expected	No dose adjustment needed.
	ETR	ETR AUC ↑ 86%	No dose adjustment needed.
	NVP	NVP AUC ↑ 110%	Consider alternative ARV or antifungal agent. Increased risk of hepatotoxicity possible with this combination.
Isavuconazole	DOR, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
Itraconazole	DOR, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV	Itraconazole and OH-itraconazole AUC, C _{max} , and C _{min} ↓ 35% to 44%	Do not coadminister, unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.
	NVP	Itraconazole AUC ↓ 61% ↑ NVP possible	Do not coadminister, unless potential benefits outweigh the risks. If coadministration is necessary, monitor itraconazole concentration and adjust dose accordingly.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 6 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Posaconazole	DOR, ETR, NVP, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	Do not coadminister, unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
Voriconazole	DOR, RPV	↑ NNRTI possible	No dose adjustment needed.
	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	Contraindicated at standard doses. Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed.
	NVP	↓ voriconazole possible ↑ NVP possible	Consider alternative ARV or antifungal agent. If coadministration is necessary, monitor antiretroviral tolerability and antifungal response and/or voriconazole concentration.
Antimalarials			
Artemether/ Lumefantrine	DOR, RPV	↔ antimalarial expected	No dose adjustment needed.
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor for antimalarial efficacy.
	NVP	Artemether AUC ↓ 67% to 72% DHA: • Study results are conflicting. DHA AUC ↓ 37% in one study, no difference in another. Lumefantrine: • Study results are conflicting. Lumefantrine AUC ↓ 25% to 58% in two studies but ↑ 56% in another.	Clinical significance unknown. If used in combination, monitor closely for antimalarial efficacy and lumefantrine toxicity.
Atovaquone/ Proguanil	DOR, ETR, NVP, RPV	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 7 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiplatelets			
Clopidogrel	DOR, NVP, RPV	↔ clopidogrel expected	No dose adjustment needed.
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed.
Ticagrelor	DOR, RPV	↔ ticagrelor expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, NVP, RPV	↔ vorapaxar expected	No dose adjustment needed.
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Anti-Toxoplasmosis Drugs			
Atovaquone (oral solution)	DOR, ETR, RPV, NVP	No data	Monitor for therapeutic effectiveness of atovaquone.
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Cardiac Medications			
Dihydropyridine CCBs	DOR, RPV	↔ CCBs expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem, Verapamil	DOR, RPV	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed.
	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR, NVP	↓ diltiazem or verapamil possible	
Corticosteroids			
Dexamethasone	DOR, EFV, ETR, NVP	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	Contraindicated with more than a single dose of dexamethasone.
Glucose-Lowering Agents			
Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin	All NNRTIs	↔ antihyperglycemic expected	No dose adjustment needed.
Linagliptin, Saxagliptin	DOR, RPV	↔ antihyperglycemic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C _{max} ↓ 24%	No dose adjustment needed.
	EFV, ETR, NVP, RPV	↔ metformin expected	No dose adjustment needed.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 8 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	DOR, RPV	No data	No dose adjustment needed.
	EFV, ETR, NVP	Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared with Daclatasvir 60 mg Alone: • Daclatasvir C_{min} ↓ 17% and AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
Dasabuvir plus Paritaprevir/Ombitasvir/RTV	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	No data	Contraindicated.
	ETR, NVP	↓ DAAs possible	Do not coadminister.
	RPV	RPV AUC ↑ 150% to 225%	Do not coadminister , due to potential for QT interval prolongation with higher concentrations of RPV.
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed.
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	Contraindicated.
	ETR, NVP	↓ elbasvir and grazoprevir expected	Do not coadminister.
	RPV	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed.
Glecaprevir/Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed.
	EFV	↓ glecaprevir and pibrentasvir expected	Do not coadminister.
	ETR	↓ glecaprevir and pibrentasvir possible	
	NVP	↓ glecaprevir and pibrentasvir possible	Consider alternative ARV or HCV regimen. If coadministration is necessary, monitor for HCV treatment efficacy.
	RPV	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed.
Ledipasvir/Sofosbuvir	DOR, RPV	↔ ledipasvir and sofosbuvir ↔ DOR ↔ RPV	No dose adjustment needed.
	EFV	Ledipasvir AUC, C_{min} , and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR, NVP	No significant effect expected	
Sofosbuvir/Velpatasvir	DOR, RPV	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	Do not coadminister.
	ETR, NVP	↓ velpatasvir expected	Do not coadminister.
Sofosbuvir/Velpatasvir/Voxilaprevir	DOR, RPV	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47% ↓ voxilaprevir expected	Do not coadminister.
	ETR, NVP	↓ voxilaprevir expected ↓ velpatasvir expected	Do not coadminister.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 9 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Herbal Products			
St. John's Wort	DOR, RPV	↓ NNRTI expected	Contraindicated.
	EFV, ETR, NVP	↓ EFV, ETR, and NVP expected	Do not coadminister.
Hormonal Therapies			
Contraceptives –Injectable Depot MPA	DOR, ETR, RPV	↔ MPA expected	No dose adjustment needed.
	EFV, NVP	↔ MPA	No dose adjustment needed.
Contraceptives – Oral	DOR	↔ ethinyl estradiol ↔ levonorgestrel	No dose adjustment needed.
	EFV	↔ ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C _{min} ↓ 61% Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64%	When Used for Contraception: • Use alternative ARV or contraceptive methods. When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation): • Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone	No dose adjustment needed.
	NVP	Ethinyl estradiol AUC ↓ 29% and C _{min} ↓ 58% Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C _{min} ↓ 22%	No dose adjustment needed based on clinical data that demonstrated no change in effectiveness
	RPV	↔ ethinyl estradiol ↔ norethindrone	No dose adjustment needed.
Contraceptives – Subdermal Implant Etonogestrel	DOR, RPV	↔ etonogestrel expected	No dose adjustment needed.
	EFV	Etonogestrel AUC ↓ 63% to 82%	Use alternative ARV or contraceptive methods.
	ETR	↓ etonogestrel possible	No data available to make dose recommendation.
	NVP	↔ etonogestrel	No dose adjustment needed.
Contraceptives –Subdermal Implant Levonorelrel	DOR, RPV	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 47%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
	NVP	Levonorgestrel AUC ↑ 35%	No dose adjustment needed.
Contraceptives – Vaginal Ring Etonogestrel/ Ethinyl Estradiol	DOR, RPV	↔ etonogestrel and ethinyl estradiol expected	No dose adjustment needed.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Contraceptives – Vaginal Ring Etonogestrel/ Ethinyl Estradiol	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Consider alternative ARV or contraceptive method.
	ETR, NVP	↓ etonogestrel and ethinyl estradiol possible	No data available to make dose recommendation.
Contraceptives – Vaginal Ring	DOR, RPV	↔ segesterone and ethinyl estradiol expected	No dose adjustment needed.
Segesterone/ Ethinyl Estradiol	EFV, ETR, NVP	↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.
	NVP, ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
Gender-Affirming Therapy	DOR, RPV	↔ hormonal concentrations expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ estradiol possible ↔ goserelin, leuprolide acetate, and spironolactone expected ↓ dutasteride and finasteride possible	Monitor feminizing effects of estrogen and antiandrogen therapy and titrate dose as necessary to achieve therapeutic goals.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone and titrate testosterone dose as necessary to achieve therapeutic goals.
Menopausal Replacement Therapy	DOR, RPV	↔ hormonal concentrations expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives – Oral for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
Immunosuppressants			
Cyclosporine	DOR, RPV	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV	↔ immunosuppressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 11 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying Agents			
Atorvastatin	DOR, RPV	↔ atorvastatin AUC	No dose adjustment needed.
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	NVP	↓ atorvastatin possible	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Fluvastatin	DOR, NVP, RPV	↔ fluvastatin expected	No dose adjustment needed.
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	DOR, RPV	↔ lovastatin and simvastatin expected	No dose adjustment needed.
	EFV	Simvastatin AUC ↓ 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, NVP, RPV	↔ pitavastatin expected	No dose adjustment needed.
	EFV	↔ pitavastatin AUC	No dose adjustment needed.
Pravastatin	DOR, NVP, RPV	↔ pravastatin expected	No dose adjustment needed.
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, NVP, RPV	↔ rosuvastatin expected	No dose adjustment needed.
Narcotics/Treatments for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV	↔ buprenorphine expected	No dose adjustment needed.
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed; monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed.
	NVP	No significant effect	No dose adjustment needed.
Buprenorphine Implant	DOR, RPV	↔ buprenorphine expected	No dose adjustment needed.
	EFV, ETR, NVP	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, NVP, RPV	↔ lofexidine expected	No dose adjustment needed.
Methadone	DOR, ETR	No significant effect	No dose adjustment needed.
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	NVP	Methadone AUC ↓ 37% to 51% ↔ NVP	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	RPV	R-methadone ^a AUC ↓ 16%	No dose adjustment needed, but monitor for withdrawal symptoms.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 12 of 12)

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors			
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed.
	EFV, NVP	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV	↔ sildenafil AUC and C _{max}	No dose adjustment needed.
Tadalafil	DOR, RPV	↔ tadalafil expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ tadalafil possible	May need to titrate tadalafil dose based on clinical effect.
Avanafil, Vardenafil	DOR, RPV	↔ avanafil or vardenafil expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ avanafil or vardenafil possible	May need to increase PDE5 inhibitor dose based on clinical effect.

^a R-methadone is the active form of methadone.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: ARV = antiretroviral; AUC = area under the curve; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DLV = delavirdine; DOR = doravirine; EFV = efavirenz; ETR = etravirine; FDA = Food and Drug Administration; HCV = hepatitis C virus; INR = international normalized ratio; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 3)

This table provides information on the known or predicted interactions between NRTIs and non-ARV drugs. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Note: Interactions associated with ddI and d4T are **not** included in this table. Please refer to the FDA product labels for ddI and d4T for information regarding drug interactions between these NRTIs and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cytomegalovirus and Hepatitis B Antivirals			
Adefovir	TAF, TDF	No data	Do not coadminister. Serum concentrations of TDF and/or other renally eliminated drugs may increase.
Ganciclovir, Valganciclovir	TAF, TDF	No data	Serum concentrations of ganciclovir and/or TFV may increase. Monitor for dose-related toxicities.
	ZDV	↔ ZDV expected ↔ ganciclovir expected	If coadministered, closely monitor for hematologic toxicities.
Hepatitis C Antiviral Agents			
Glecaprevir/ Pibrentasvir	TAF	↔ TFV AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 29%	No dose adjustment needed.
Ledipasvir/ Sofosbuvir	TAF	TFV AUC ↑ 27%	No dose adjustment needed.
	TDF	Ledipasvir ↑ TFV AUC 40% to 98% when TDF is given with RPV and EFV Ledipasvir ↑ TFV C _{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs Further ↑ TFV AUC and C _{max} possible when TDF is given with PIs	Do not coadminister with EVG/c/TDF/FTC. If TDF is used in these patients, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	TDF	Ribavirin With Sofosbuvir 400 mg: • ↔ TFV AUC	No dose adjustment needed.
	ZDV	Ribavirin inhibits phosphorylation of ZDV	Consider alternative. If coadministered, closely monitor HIV virologic response and monitor for possible hematologic toxicities.
Sofosbuvir/ Velpatasvir	TAF	↔ TAF expected	No dose adjustment needed.
	TDF	TFV C _{max} and AUC ↑ 39% to 81% when coadministered with various ARV combinations	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/ Velpatasvir/ Voxilaprevir	TAF	↔ TAF expected	No dose adjustment needed.
	TDF	TFV C _{max} and AUC ↑ 35% to 55% when coadministered with various ARV combinations	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 3)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
INSTIs			
DTG	TAF	↔ TAF AUC	No dose adjustment needed.
	TDF	↔ TDF AUC	No dose adjustment needed.
		↔ DTG AUC	
RAL	TDF	RAL AUC ↑ 49%	No dose adjustment needed.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	3TC, TDF, ZDV	↔ 3TC, TDF, ZDV, and buprenorphine	No dose adjustment needed.
	TAF	↔ TAF expected	No dose adjustment needed.
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment needed.
	ZDV	ZDV AUC ↑ 29% to 43%	Monitor for ZDV-related adverse effects.
Other			
Anticonvulsants Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With Carbamazepine: • TAF AUC ↓ 55% ↓ TAF possible with other anticonvulsants	Do not coadminister.
Antimycobacterial Rifampin	TAF	TAF with Rifampin Compared with TDF Alone: • TFV-DP AUC ↑ 4.2-fold TAF with Rifampin Compared with TAF Alone: • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% TAF 25 mg Twice Daily with Rifampin Compared with TAF Once Daily Alone: • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	Do not coadminister, unless benefits outweigh risks. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin compared to TDF administered alone, but clinical outcomes have not been studied. If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Atovaquone	ZDV	ZDV AUC ↑ 31%	Monitor for ZDV-related adverse effects.
Rifabutin, Rifapentine	TAF	↓ TAF possible	Do not coadminister.
St. John's Wort	TAF	↓ TAF possible	Do not coadminister.
PIs for Treatment of HIV			
ATV (Unboosted), ATV/c, ATV/r	TAF	TAF 10 mg with ATV/r: • TAF AUC ↑ 91% TAF 10 mg with ATV/c: • TAF AUC ↑ 75%	No dose adjustment needed (use TAF 25 mg).

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 3)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
ATV (Unboosted), ATV/c, ATV/r	TDF	With ATV (Unboosted): • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) TFV AUC ↑ 24% to 37%	Do not coadminister unboosted ATV with TDF. Use ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities.
	ZDV	With ATV (Unboosted): • ZDV C_{min} ↓ 30% and ↔ ZDV AUC	Clinical significance unknown. If coadministered, monitor virologic response.
DRV/c	TAF	TAF 25 mg with DRV/c: • ↔ TAF	No dose adjustment needed.
	TDF	↑ TFV possible	Monitor for TDF-associated toxicities.
DRV/r	TAF	TAF 10 mg with DRV/r: • ↔ TAF AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities.
LPV/r	TAF	TAF 10 mg with DRV/r: • TAF AUC ↑ 47%	No dose adjustment needed.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities.
TPV/r	ABC	ABC AUC ↓ 35% to 44%	Clinical significance unknown. If coadministered, monitor virologic response.
	TAF	↓ TAF expected	Do not coadminister, unless benefits outweigh risks.
	TDF	↔ TDF AUC TPV AUC ↓ 9% to 18% and C_{min} ↓ 12% to 21%	No dose adjustment needed.
	ZDV	ZDV AUC ↓ 31% to 42% ↔ TPV AUC	Clinical significance unknown. If coadministered, monitor virologic response.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 17)

This table provides information on the known or predicted interactions between INSTIs (BIC, DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. For information regarding interactions between INSTIs and other ARV drugs, including dosing recommendations, refer to Tables [21c](#), [22a](#), and [22b](#).

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. **In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.**

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Al, Mg, +/- Ca-Containing Antacids Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins).	BIC	Al/Mg Hydroxide Antacid: <ul style="list-style-type: none"> • ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions • BIC AUC ↓ 52% if antacid is administered 2 hours before BIC • BIC AUC ↓ 47% to 79% if administered simultaneously with antacid CaCO₃ Antacid: <ul style="list-style-type: none"> • ↔ BIC AUC if administered with food • BIC AUC ↓ 33% if administered under fasting conditions 	With Antacids That Contain Al/Mg: <ul style="list-style-type: none"> • Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC. With Antacids That Contain Ca: <ul style="list-style-type: none"> • Administer BIC and antacids that contain Ca together with food. • Do not coadminister BIC simultaneously with antacids that contain Ca on an empty stomach.
	DTG	DTG AUC ↓ 74% if administered simultaneously with antacid DTG AUC ↓ 26% if administered 2 hours before antacid	Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if administered simultaneously with antacid EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with 4-hour interval	Separate EVG/c and antacid administration by more than 2 hours.
	RAL	Al/Mg Hydroxide Antacid: <ul style="list-style-type: none"> • RAL C_{min} ↓ 49% to 63% CaCO₃ Antacid: <ul style="list-style-type: none"> • RAL 400 mg twice daily: C_{min} ↓ 32% • RAL 1,200 mg once daily: C_{min} ↓ 48% to 57% 	Do not coadminister RAL and Al/Mg hydroxide antacids. Use alternative acid-reducing agent. With CaCO₃ Antacids: <ul style="list-style-type: none"> • RAL 1,200 mg once daily: Do not coadminister. • RAL 400 mg twice daily: No dose adjustment or separation needed.
H2-Receptor Antagonists	BIC, DTG, EVG/c	↔ INSTI	No dose adjustment needed.
	RAL	RAL AUC ↑ 44% and C _{max} ↑ 60%	No dose adjustment needed.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers, continued			
Proton Pump Inhibitors	BIC, DTG, EVG/c	↔ INSTI	No dose adjustment needed.
	RAL	RAL AUC ↑ 37% and C _{min} ↑ 24%	No dose adjustment needed.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	BIC, DTG, RAL	↔ alfuzosin expected	No dose adjustment needed.
	EVG/c	↑ alfuzosin expected	Contraindicated.
Doxazosin	BIC, DTG, RAL	↔ doxazosin expected	No dose adjustment needed.
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate based on doxazosin efficacy and adverse events. Doxazosin dose reduction may be needed.
Tamsulosin	BIC, DTG, RAL	↔ tamsulosin expected	No dose adjustment needed.
	EVG/c	↑ tamsulosin expected	Do not coadminister, unless benefits outweigh risks. If coadministered, monitor for tamsulosin-related adverse events.
Terazosin	BIC, DTG, RAL	↔ terazosin expected	No dose adjustment needed.
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose and titrate based on terazosin efficacy and adverse events. Terazosin dose reduction may be necessary.
Silodosin	BIC, DTG, RAL	↔ silodosin expected	No dose adjustment needed.
	EVG/c	↑ silodosin expected	Contraindicated.
Antibacterials			
Antimycobacterials			
Rifabutin	BIC	Rifabutin 300 mg Once Daily: • BIC AUC ↓ 38% and C _{min} ↓ 56%	Do not coadminister.
	DTG	Rifabutin 300 mg Once Daily: • ↔ DTG AUC and C _{min} ↓ 30%	No dose adjustment needed.
	EVG/c	Rifabutin 150 mg Every Other Day with EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone: • ↔ rifabutin AUC • 25-O-desacetyl-rifabutin AUC ↑ 625% • EVG AUC ↓ 21% and C _{min} ↓ 67%	Do not coadminister.
	RAL	RAL AUC ↑ 19% and C _{min} ↓ 20%	No dose adjustment needed.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, continued			
Rifampin	BIC	BIC AUC ↓ 75%	Contraindicated.
	DTG	Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone: <ul style="list-style-type: none"> DTG AUC ↓ 54% and C_{min} ↓ 72% Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone: <ul style="list-style-type: none"> DTG AUC ↑ 33% and C_{min} ↑ 22% 	Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations. Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations.
	EVG/c	Significant ↓ EVG and COBI expected	Contraindicated.
	RAL	RAL 400 mg: <ul style="list-style-type: none"> RAL AUC ↓ 40% and C_{min} ↓ 61% Rifampin with RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone: <ul style="list-style-type: none"> RAL AUC ↑ 27% and C_{min} ↓ 53% 	Use RAL 800 mg twice daily instead of 400 mg twice daily. Do not coadminister RAL 1,200 mg once daily with rifampin. Monitor closely for virologic response, or consider using rifabutin as an alternative rifamycin.
Rifapentine	BIC, DTG, EVG/c	Significant ↓ BIC, DTG, EVG, and COBI expected	Do not coadminister.
	RAL	Rifapentine 900 mg Once Weekly: <ul style="list-style-type: none"> RAL AUC ↑ 71% and C_{min} ↓ 12% Rifapentine 600 mg Once Daily: <ul style="list-style-type: none"> RAL C_{min} ↓ 41% 	For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment needed. Do not coadminister with once-daily rifapentine.
Macrolides			
Azithromycin	All INSTIs	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	BIC	↑ BIC possible	No dose adjustment needed.
	DTG, RAL	↔ clarithromycin expected	No dose adjustment needed.
	EVG/c	↑ clarithromycin expected ↑ COBI possible	Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min. Do not coadminister in patients with CrCl <50 mL/min. Consider alternative ARV or use azithromycin.
Erythromycin	BIC	↑ BIC possible	No dose adjustment needed.
	DTG, RAL	↔ INSTI expected ↔ erythromycin expected	No dose adjustment needed.
	EVG/c	↑ erythromycin expected ↑ COBI possible	No data available for dose recommendation. Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	BIC, DTG, RAL	↔ apixaban expected	No dose adjustment needed.
	EVG/c	↑ apixaban expected	Do not coadminister in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants, continued			
Betrixaban	BIC, DTG, RAL	↔ betrixaban expected	No dose adjustment needed.
	EVG/c	↑ betrixaban expected	Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily.
Dabigatran	BIC, DTG, RAL	↔ dabigatran expected	No dose adjustment needed.
	EVG/c	↑ dabigatran expected With COBI 150 mg Alone: • Dabigatran AUC ↑ 110% to 127%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.
Edoxaban	BIC, DTG, RAL	↔ edoxaban expected	No dose adjustment needed.
	EVG/c	↔ or ↑ edoxaban expected	Stroke Prevention in Nonvalvular Atrial Fibrillation: • No dose adjustment needed. Deep Venous Thrombosis and Pulmonary Embolism: • Administer edoxaban 30 mg once daily.
Rivaroxaban	BIC, DTG, RAL	↔ rivaroxaban expected	No dose adjustment needed.
	EVG/c	↑ rivaroxaban expected	Do not coadminister.
Warfarin	BIC, DTG, RAL	↔ warfarin expected	No dose adjustment needed.
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine	BIC	↓ BIC possible	Do not coadminister.
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg twice daily in ART-naïve or ART-experienced, INSTI-naïve patients. Do not coadminister in INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C _{min} ↓ >99% ↓ COBI expected	Contraindicated.
	RAL	↓ or ↔ RAL possible	Do not coadminister.
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider alternative ARV or anticonvulsant.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants, continued			
Ethosuximide	BIC, DTG, RAL	↔ ethosuximide expected	No dose adjustment needed.
	EVG/c	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	BIC, DTG, RAL	↔ lamotrigine expected	No dose adjustment needed.
	EVG/c	No data	Monitor anticonvulsant concentrations and adjust dose accordingly.
Oxcarbazepine	BIC, DTG	↓ BIC and DTG possible	Do not coadminister.
	EVG/c, RAL	↓ EVG/c and RAL possible	Consider alternative ARV or anticonvulsant.
Phenobarbital Phenytoin	BIC	↓ BIC possible	Do not coadminister.
	DTG	↓ DTG possible	Do not coadminister.
	EVG/c	↓ EVG/c expected	Contraindicated.
	RAL	↓ or ↔ RAL possible	Do not coadminister.
Valproic Acid	All INSTIs	No data	Monitor valproic acid concentration and virologic response.
Antidepressants, Anxiolytics, Antipsychotics			
Also see Sedative/Hypnotics section below			
Aripiprazole	BIC, DTG, RAL	↔ aripiprazole expected	No dose adjustment needed.
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole efficacy and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Brexipiprazole	BIC, DTG, RAL	↔ brexpiprazole expected	No dose adjustment needed.
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole efficacy and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Bupropion	BIC, DTG, RAL	↔ bupropion expected	No dose adjustment needed.
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, DTG, RAL	↔ buspirone expected	No dose adjustment needed.
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Buspirone dose reduction may be needed.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 6 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, Antipsychotics, continued			
Also see Sedative/Hypnotics section below			
Cariprazine	BIC, DTG, RAL	↔ cariprazine expected	No dose adjustment needed.
	EVG/c	↑ cariprazine expected	<p>Starting Cariprazine in a Patient Who Is Already Receiving EVG/c:</p> <ul style="list-style-type: none"> Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased. <p>Starting EVG/c in a Patient Who is Already Receiving Cariprazine:</p> <ul style="list-style-type: none"> For patients receiving cariprazine 3 mg or 6 mg daily, reduce cariprazine dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to 1.5 mg or 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased.
Iloperidone	BIC, DTG, RAL	↔ iloperidone expected	No dose adjustment needed.
	EVG/c	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lurasidone	BIC, DTG, RAL	↔ lurasidone expected	No dose adjustment needed.
	EVG/c	↑ lurasidone expected	Contraindicated.
Nefazodone	BIC, DTG, RAL	↔ nefazodone expected	No dose adjustment needed.
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.
Pimavanserin	BIC, DTG, RAL	↔ pimavanserin expected	No dose adjustment needed.
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg.
Pimozide	BIC, DTG, RAL	↔ pimozide expected	No dose adjustment needed.
	EVG/c	↑ pimozide expected	Contraindicated.
Quetiapine	BIC, DTG, RAL	↔ quetiapine expected	No dose adjustment needed.
	EVG/c	↑ quetiapine AUC expected	<p>Starting Quetiapine in a Patient Receiving EVG/c:</p> <ul style="list-style-type: none"> Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. <p>Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine:</p> <ul style="list-style-type: none"> Reduce quetiapine dose to 1/6 of the current dose, and closely monitor for quetiapine efficacy and adverse events.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 7 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, Antipsychotics, continued			
Also see Sedative/Hypnotics section below			
Selective Serotonin Reuptake Inhibitors Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	EVG/c	↔ EVG	No dose adjustment needed.
		↔ sertraline	
		↑ other SSRIs possible	Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response.
	BIC, DTG, RAL	↔ BIC, DTG and RAL expected ↔ SSRI expected	No dose adjustment needed.
Tricyclic Antidepressants Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	BIC, DTG, RAL	↔ TCA expected	No dose adjustment needed.
	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA and titrate dose carefully based on antidepressant response and/or drug concentrations.
Trazodone	BIC, DTG, RAL	↔ trazodone expected	No dose adjustment needed.
	EVG/c	↑ trazodone possible	Initiate with lowest dose of trazodone and titrate dose carefully.
Ziprasidone	BIC, DTG, RAL	↔ ziprasidone expected	No dose adjustment needed.
	EVG/c	↑ ziprasidone possible	Monitor for ziprasidone-related adverse events.
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.
Antifungals			
Isavuconazole	BIC	↑ BIC possible	No dose adjustment needed.
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assessing virologic response.
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed.
	DTG, RAL	↔ INSTI expected ↔ itraconazole expected	No dose adjustment needed.
	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. Do not coadminister with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 8 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Posaconazole	BIC	↑ BIC expected	No dose adjustment needed.
	DTG, RAL	↔ INSTI expected ↔ posaconazole expected	No dose adjustment needed.
	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment needed.
	DTG, RAL	↔ INSTI expected ↔ voriconazole expected	No dose adjustment needed.
	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	Do not coadminister voriconazole and COBI unless benefit outweighs risk. If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.
Antihyperglycemics			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	DTG	DTG 50 mg Once Daily plus Metformin 500 mg Twice Daily: • Metformin AUC ↑ 79% and C _{max} ↑ 66% DTG 50 mg Twice Daily plus Metformin 500 mg Twice Daily: • Metformin AUC ↑ 2.4-fold and C _{max} ↑ 2-fold	Start metformin at lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.
	RAL	↔ metformin expected	No dose adjustment needed.
Saxagliptin	BIC, DTG, RAL	↔ saxagliptin expected	No dose adjustment needed.
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	BIC, DTG, RAL	↔ dapagliflozin or saxagliptin expected	No dose adjustment needed.
	EVG/c	↑ saxagliptin expected	Do not coadminister. Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination is not recommended.
Antiplatelets			
Clopidogrel	BIC, DTG, RAL	↔ clopidogrel expected	No dose adjustment needed.
	EVG/c	↓ clopidogrel active metabolite, with impaired platelet inhibition expected	Do not coadminister.
Prasugrel	BIC, DTG, RAL	↔ prasugrel expected	No dose adjustment needed.
	EVG/c	↓ prasugrel active metabolite, with no impairment of platelet inhibition expected	Insufficient data to make a dose recommendation.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 9 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiplatelets, continued			
Ticagrelor	BIC, DTG, RAL	↔ ticagrelor expected	No dose adjustment needed.
	EVG/c	↑ ticagrelor expected	Do not coadminister.
Vorapaxar	BIC, DTG, RAL	↔ vorapaxar expected	No dose adjustment needed.
	EVG/c	↑ vorapaxar expected	Do not coadminister.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed.
Indacaterol	BIC, DTG, RAL	↔ indacaterol expected	No dose adjustment needed.
	EVG/c	↑ indacaterol expected	
Olodaterol	BIC, DTG, RAL	↔ olodaterol expected	No dose adjustment needed.
	EVG/c	↑ olodaterol expected	
Salmeterol	BIC, DTG, RAL	↔ salmeterol expected	No dose adjustment needed.
	EVG/c	↑ salmeterol possible	Do not coadminister because of potential increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Amiodarone	BIC, DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed.
	EVG/c	↑ INSTI possible ↑ amiodarone possible	Do not coadminister, unless benefits outweigh risks. If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations.
Bepidil, Digoxin, Disopyramide, Dronedarone, Flecainide, Systemic Lidocaine, Mexilitine, Propafenone, Quinidine	BIC, DTG	↔ expected for the listed antiarrhythmics, except for disopyramide ↑ disopyramide possible	No dose adjustment needed. Monitor for disopyramide-related adverse events.
	RAL	↔ expected for the listed antiarrhythmics	No dose adjustment needed.
	EVG/c	↑ antiarrhythmics possible Digoxin C _{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for antiarrhythmics, if available, is recommended.
Beta-Blockers (e.g., metoprolol, timolol)	BIC, DTG, RAL	↔ beta-blocker expected	No dose adjustment needed.
	EVG/c	↑ beta-blocker possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response. Consider using an alternative ARV, or a beta-blocker that is not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications, continued			
Bosentan	BIC, DTG	↓ BIC and DTG possible	No dose adjustment needed.
	RAL	↔ bosentan expected	No dose adjustment needed.
	EVG/c	↑ bosentan possible	In Patients on EVG/c ≥10 Days: • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. In Patients on Bosentan Who Require EVG/c: • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed.
	DTG, RAL	↔ INSTI expected ↔ CCB expected	No dose adjustment needed.
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Dofetilide	BIC, DTG	↑ dofetilide expected	Contraindicated.
	RAL	↔ dofetilide expected	No dose adjustment needed.
	EVG/c	↑ dofetilide possible	Do not coadminister.
Eplerenone	BIC, DTG, RAL	↔ eplerenone expected	No dose adjustment needed.
	EVG/c	↑ eplerenone expected	Contraindicated.
Ivabradine	BIC, DTG, RAL	↔ ivabradine expected	No dose adjustment needed.
	EVG/c	↑ ivabradine expected	Contraindicated.
Ranolazine	BIC, DTG, RAL	↔ ranolazine expected	No dose adjustment needed.
	EVG/c	↑ ranolazine expected	Contraindicated.
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed.
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	BIC, DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed.
	EVG/c	↑ glucocorticoid possible	Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone).

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 11 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids, continued			
Betamethasone, Budesonide Systemic	BIC, DTG, RAL	↔ INSTI expected ↔ glucocorticoid expected	No dose adjustment needed.
	EVG/c	↑ glucocorticoids possible ↓ EVG possible	Do not coadminister unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	BIC	↓ BIC possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
	DTG, RAL	↔ INSTI expected	No dose adjustment needed.
	EVG/c	↓ EVG and COBI possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	BIC, DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed.
	EVG/c	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing's syndrome.
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	BIC, DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed.
	EVG/c	↑ glucocorticoid expected	Do not coadminister. Coadministration may result in adrenal insufficiency and Cushing's syndrome.
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	BIC, RAL	No data	No dose adjustment needed.
	DTG	↔ daclatasvir	No dose adjustment needed.
	EVG/c	↑ daclatasvir	Decrease daclatasvir dose to 30 mg once daily.
Dasabuvir plus Ombitasvir/Paritaprevir/RTV	BIC, DTG	No data	No dose adjustment needed.
	EVG/c	No data	Do not coadminister.
	RAL	RAL AUC ↑ 134%	No dose adjustment needed.
Elbasvir/Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed.
	DTG	↔ elbasvir ↔ grazoprevir ↔ DTG	No dose adjustment needed.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 12 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Elbasvir/Grazoprevir	EVG/c	↑ elbasvir expected ↑ grazoprevir expected	Do not coadminister.
	RAL	↔ elbasvir ↔ grazoprevir ↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir	No dose adjustment needed.
Glecaprevir/Pibrentasvir	BIC	↔ BIC expected	No dose adjustment needed.
	DTG, RAL	No significant effect	No dose adjustment needed.
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57% EVG AUC ↑ 47%	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
Ledipasvir/Sofosbuvir	BIC, DTG, RAL	↔ DTG and RAL	No dose adjustment needed.
	EVG/c/ TDF/FTC	↑ TDF expected ↑ ledipasvir expected	Do not coadminister.
	EVG/c/ TAF/FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment needed.
Sofosbuvir	All INSTIs	↔ INSTI expected ↔ sofosbuvir expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir	All INSTIs	↔ INSTI expected ↔ sofosbuvir and velpatasvir expected	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	EVG/c	When Administered with Sofosbuvir/ Velpatasvir/Voxilaprevir (400 mg/100 mg/100 mg) plus Voxilaprevir 100 mg: • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
	BIC, DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed.
Herbal Products			
St. John's Wort	BIC, DTG	↓ BIC and DTG possible	Do not coadminister.
	EVG/c	↓ EVG and COBI expected	Contraindicated.
Hormonal Therapies			
Contraceptives: Non-Oral	All INSTIs	No data	No drug-drug interaction studies have been conducted with INSTIs and non-oral routes of hormone administration. It is unclear whether drug-drug interaction data for oral drugs can be used to predict interactions for non-oral drugs.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 13 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Contraceptives – Oral	BIC, DTG, RAL	↔ ethinyl estradiol and norgestimate ↔ INSTI	No dose adjustment needed.
	EVG/c	Norgestimate AUC, C_{max} , and C_{min} ↑ >2-fold Ethinyl estradiol AUC ↓ 25% and C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended, due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.
Gender-Affirming Therapy	BIC, DTG, EVG/c, RAL	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed.
	BIC, DTG, RAL	↔ estrogen expected	No dose adjustment needed.
		↔ testosterone expected	No dose adjustment needed.
	EVG/c	↓ or ↑ estradiol possible ↑ dutasteride and finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations.
		↑ testosterone possible	Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.
Menopausal Replacement Therapy	BIC, DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, medroxyprogesterone, and micronized progesterone expected	No dose adjustment needed.
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral medroxyprogesterone possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, DTG, RAL	↔ immunosuppressant expected	No dose adjustment needed.
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying Agents			
Atorvastatin	BIC, DTG, RAL	↔ atorvastatin expected	No dose adjustment needed.
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C_{max} ↑ 2.3-fold	Titrate statin dose carefully and administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 14 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying Agents , continued			
Lomitapide	BIC, DTG, RAL	↔ lomitapide expected	No dose adjustment needed.
	EVG/c	↑ lomitapide expected	Contraindicated.
Lovastatin	BIC, DTG, RAL	↔ lovastatin expected	No dose adjustment needed.
	EVG/c	Significant ↑ lovastatin expected	Contraindicated.
Pitavastatin, Pravastatin	BIC, DTG, RAL	↔ statin expected	No dose adjustment needed.
	EVG/c	No data	No data available for dose recommendation.
Rosuvastatin	BIC, DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed.
	EVG/c	Rosuvastatin AUC ↑ 38% and C _{max} ↑ 89%	Titrate statin dose carefully and use the lowest effective dose while monitoring for adverse events.
Simvastatin	BIC, DTG, RAL	↔ simvastatin expected	No dose adjustment needed.
	EVG/c	Significant ↑ simvastatin expected	Contraindicated.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	BIC, DTG	↔ buprenorphine and norbuprenorphine (active metabolite) expected	No dose adjustment needed.
	EVG/c	Buprenorphine AUC ↑ 35% and C _{min} ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 42% and C _{min} ↑ 57%	No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual) ↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)	No dose adjustment needed.
Fentanyl	BIC, DTG, RAL	↔ fentanyl expected	No dose adjustment needed.
	EVG/c	↑ fentanyl	Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.
Lofexidine	BIC, DTG, RAL	↔ lofexidine expected	No dose adjustment needed.
	EVG/c	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	All INSTIs	↔ methadone	No dose adjustment needed.
Tramadol	BIC, DTG, RAL	↔ tramadol and M1 (active metabolite) expected	No dose adjustment needed.
	EVG/c	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.

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Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors			
Avanafil	BIC, DTG, RAL	↔ avanafil expected	No dose adjustment needed.
	EVG/c	No data	Do not coadminister.
Sildenafil	BIC, DTG, RAL	↔ sildenafil expected	No dose adjustment needed.
	EVG/c	↑ sildenafil expected	For Treatment of Erectile Dysfunction: • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. Contraindicated for treatment of PAH.
Tadalafil	BIC, DTG, RAL	↔ tadalafil expected	No dose adjustment needed.
	EVG/c	↑ tadalafil expected	For Treatment of Erectile Dysfunction: • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For Treatment of PAH <i>In Patients on EVG/c >7 Days:</i> • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. <i>In Patients on Tadalafil who Require EVG/c:</i> • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily, and increase to tadalafil 40 mg once daily based on tolerability.
Vardenafil	BIC, DTG, RAL	↔ vardenafil expected	No dose adjustment needed.
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedative/Hypnotics			
Buspirone	BIC, DTG, RAL	↔ buspirone expected	No dose adjustment needed.
	EVG/c	↑ buspirone expected	Initiate buspirone at a low dose. Dose reduction may be needed.
Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, DTG, RAL	↔ benzodiazepine expected	No dose adjustment needed.
	EVG/c	↑ benzodiazepine possible	Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events. Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam.
Midazolam, Triazolam	BIC, RAL	↔ benzodiazepine expected	No dose adjustment needed.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 16 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sedative/Hypnotics, continued			
Midazolam, Triazolam, continued	DTG	With DTG 25 mg: • ↔ midazolam AUC	No dose adjustment needed.
	EVG/c	↑ midazolam expected ↑ triazolam expected	Contraindicated. Do not coadminister triazolam or oral midazolam and EVG/c. Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.
Suvorexant	BIC, DTG, RAL	↔ suvorexant expected	No dose adjustment needed.
	EVG/c	↑ suvorexant expected	Do not coadminister.
Zolpidem	BIC, DTG, RAL	↔ zolpidem expected	No dose adjustment needed.
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary.
Miscellaneous Drugs			
Calcifediol	BIC, DTG, RAL	↔ calcifediol expected	No dose adjustment needed.
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations.
Cisapride	BIC, DTG, RAL	↔ cisapride expected	No dose adjustment needed.
	EVG/c	↑ cisapride expected	Contraindicated.
Colchicine	BIC, DTG, RAL	↔ colchicine expected	No dose adjustment needed.
	EVG/c	↑ colchicine expected	Do not coadminister in patients with hepatic or renal impairment. For Treatment of Gout Flares: • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For Prophylaxis of Gout Flares: • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. For Treatment of Familial Mediterranean Fever: • Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily.
Dronabinol	BIC, DTG, RAL	↔ dronabinol expected	No dose adjustment needed.
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse events.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 17 of 17)

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Drugs, continued			
Eluxadoline	BIC, DTG, RAL	↔ eluxadoline expected	No dose adjustment needed.
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse events.
Ergot Derivatives	BIC, DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed.
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Contraindicated.
Flibanserin	BIC, DTG, RAL	↔ flibanserin expected	No dose adjustment needed.
	EVG/c	↑ flibanserin expected	Contraindicated.
Polyvalent Cation Supplements Mg, Al, Fe, Ca, Zn, including multivitamins with minerals Note: Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.	BIC	↔ BIC AUC if administered simultaneously with Fe or Ca and food BIC AUC ↓ 33% if administered simultaneously with CaCO ₃ under fasting conditions BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions	With Supplements That Contain Ca or Fe: • Administer BIC and supplements that contain Ca or Fe together with food. Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	DTG	DTG AUC ↓ 39% if administered simultaneously with CaCO ₃ under fasting conditions DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	With Supplements That Contain Ca or Fe: • Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement. Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CaCO₃ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DAA = direct-acting antiviral; DTG = dolutegravir; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; HCV = hepatitis C virus; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PDE5 = Phosphodiesterase Type 5; PTH = parathyroid hormone; RAL = raltegravir; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

Table 21e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 3)

In the table below, “No dose adjustment needed” indicates that the FDA-approved dose of MVC 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Concomitant Drug Class/Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterial Agents		
Antimycobacterials		
Rifabutin	↓ MVC possible	If Used <u>Without</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • MVC 300 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • MVC 150 mg twice daily
Rifampin	MVC AUC ↓ 63%	If Used <u>Without</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • MVC 600 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • Consider alternative ARV or antimycobacterial.
Rifapentine	↓ MVC expected	Do not coadminister.
Macrolides		
Azithromycin	↔ MVC expected	No dose adjustment needed.
Clarithromycin	↑ MVC possible	MVC 150 mg twice daily
Erythromycin	↑ MVC possible	No dose adjustment needed.
Anticonvulsants		
Carbamazepine, Phenobarbital, Phenytoin	↓ MVC possible	If Used <u>Without</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • MVC 600 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: <ul style="list-style-type: none"> • MVC 150 mg twice daily
Eslicarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Oxcarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Antifungals		
Fluconazole	↑ MVC possible	No dose adjustment needed.
Isavuconazole	↑ MVC possible	No dose adjustment needed.
Itraconazole	↑ MVC possible	MVC 150 mg twice daily
Posaconazole	↑ MVC possible	MVC 150 mg twice daily
Voriconazole	↑ MVC possible	MVC 150 mg twice daily
Hepatitis C Direct-Acting Antivirals		
Daclatasvir	↔ MVC expected ↔ daclatasvir expected	No dose adjustment needed.
Dasabuvir plus Ombitasvir/ Paritaprevir/RTV	↑ MVC expected	Do not coadminister.
Elbasvir/Grazoprevir	↔ MVC expected	No dose adjustment needed.

Table 21e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 3)

Concomitant Drug Class/Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antivirals, continued		
Glecaprevir/Pibrentasvir	↔ MVC expected	No dose adjustment needed.
Ledipasvir/Sofosbuvir	↔ MVC expected	No dose adjustment needed.
Simeprevir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ MVC expected	No dose adjustment needed.
Herbal Products		
St. John's Wort	↓ MVC expected	Do not coadminister.
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed.
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed.
Gender-Affirming Hormone Therapies	↔ MVC or gender-affirming hormones expected	No dose adjustment needed.
Antiretroviral Drugs		
INSTIs		
BIC, DTG	↔ MVC expected	No dose adjustment needed.
EVG/c	↑ MVC possible	MVC 150 mg twice daily
RAL	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment needed.
NNRTIs		
DOR, RPV	↔ MVC expected	No dose adjustment needed.
EFV	MVC AUC ↓ 45%	If Used <u>Without</u> a Strong CYP3A Inhibitor: • MVC 600 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: • MVC 150 mg twice daily
ETR	MVC AUC ↓ 53%	If Used <u>Without</u> a Strong CYP3A Inhibitor: • MVC 600 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: • MVC 150 mg twice daily
NVP	↔ MVC AUC	If Used <u>Without</u> a Strong CYP3A Inhibitor: • MVC 300 mg twice daily If Used <u>With</u> a Strong CYP3A Inhibitor: • MVC 150 mg twice daily • With TPV/r, use MVC 300 mg twice daily
PIs		
ATV, ATV/c, ATV/r	With Unboosted ATV: • MVC AUC ↑ 257% With (ATV/r 300 mg/100 mg) Once Daily: • MVC AUC ↑ 388%	MVC 150 mg twice daily

Table 21e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 3)

Concomitant Drug Class/Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PIs, continued		
DRV/c, DRV/r	With (DRV/r 600 mg/100 mg) Twice Daily: • MVC AUC ↑ 305% With (DRV/r 600 mg/100 mg) Twice Daily and ETR: • MVC AUC ↑ 210%	MVC 150 mg twice daily
LPV/r	MVC AUC ↑ 295% With LPV/r and EFV: • MVC AUC ↑ 153%	MVC 150 mg twice daily
TPV/r	With (TPV/r 500 mg/200 mg) Twice Daily: • ↔ MVC AUC	No dose adjustment needed.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV/r = tipranavir/ritonavir

Table 22a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

Note: Interactions associated with DLV, FPV, IDV, NFV, and SQV are **not** included in this table. Please refer to the FDA product labels for information regarding interactions between these drugs and other concomitant drugs.

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
ATV Unboosted	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV ATV AUC ↓ 74%	ETR AUC ↑ 50% and C_{min} ↑ 58% ↔ ATV AUC and C_{min} ↓ 47%	↑ NVP possible ↓ ATV possible	↑ RPV possible ↔ ATV expected
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ NVP possible ↓ ATV possible ↓ COBI possible	↑ RPV possible ↔ ATV expected
	Dose	No dose adjustment needed.	ATV/c in ART-Naive Patients: <ul style="list-style-type: none"> • ATV 400 mg plus COBI 150 mg once daily • Do not use coformulated ATV 300 mg/ COBI 150 mg. ATV/c in ART-Experienced Patients: <ul style="list-style-type: none"> • Do not coadminister. No dose adjustment needed for EFV.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
ATV/r	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected (ATV 400 mg plus RTV 100 mg) Once Daily: <ul style="list-style-type: none"> • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV 	(ATV 300 mg plus RTV 100 mg) Once Daily: <ul style="list-style-type: none"> • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min} 	(ATV 300 mg plus RTV 100 mg) Once Daily: <ul style="list-style-type: none"> • ATV AUC ↓ 42% and C_{min} ↓ 72% • NVP AUC ↑ 25% 	↑ RPV possible ↔ ATV expected
	Dose	No dose adjustment needed.	ATV/r in ART-Naive Patients: <ul style="list-style-type: none"> • (ATV 400 mg plus RTV 100 mg) once daily ATV/r in ART-Experienced Patients: <ul style="list-style-type: none"> • Do not coadminister. No dose adjustment needed for EFV.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
DRV/c	PK Data	↑ DOR expected ↔ DRV expected	↔ EFV expected ↓ DRV possible ↓ COBI possible	ETR 400 mg Once Daily with (DRV 800 mg plus COBI 150 mg) Once Daily: <ul style="list-style-type: none"> • ↔ ETR AUC and C_{min} • ↔ DRV AUC and C_{min} ↓ 56% • COBI AUC ↓ 30% and C_{min} ↓ 66% 	↑ NVP possible ↓ DRV possible ↓ COBI possible	↔ DRV expected ↑ RPV possible
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.

Table 22a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 2)

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
DRV/r	PK Data	↑ DOR expected ↔ DRV expected	With (DRV 300 mg plus RTV 100 mg) Twice Daily: • EFV AUC ↑ 21% • ↔ DRV AUC and C _{min} ↓ 31%	ETR 100 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily: • ETR AUC ↓ 37% and C _{min} ↓ 49% • ↔ DRV	With (DRV 400 mg plus RTV 100 mg) Twice Daily: • NVP AUC ↑ 27% and C _{min} ↑ 47% • DRV AUC ↑ 24% ^a	RPV 150 mg Once Daily with (DRV 800 mg plus RTV 100 mg) Once Daily: • RPV AUC ↑ 130% and C _{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed.	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed. Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	No dose adjustment needed.	No dose adjustment needed.
LPV/r	PK Data	↑ DOR expected ↔ LPV expected	↔ EFV expected With LPV/r 500 mg/125 mg ^b Twice Daily: • LPV concentration similar to that of LPV/r 400 mg/100 mg twice daily without EFV	ETR AUC ↓ 35% (comparable to the decrease seen with DRV/r) ↔ LPV AUC	↑ NVP possible LPV AUC ↓ 27% and C _{min} ↓ 51%	RPV 150 mg Once Daily with LPV/r: • RPV AUC ↑ 52% and C _{min} ↑ 74% • ↔ LPV
	Dose	No dose adjustment needed.	LPV/r 500 mg/125 mg ^b twice daily LPV/r 533 mg/133 mg twice daily when using oral solution No dose adjustment needed for EFV.	No dose adjustment needed.	LPV/r 500 mg/125 mg ^b twice daily LPV/r 533 mg/133 mg twice daily when using oral solution No dose adjustment needed for NVP.	No dose adjustment needed.
TPV/r Note: Always use TPV with RTV	PK Data	↑ DOR expected ↔ TPV expected	With (TPV 500 mg plus RTV 100 mg) Twice Daily: • ↔ EFV • TPV AUC ↓ 31% and C _{min} ↓ 42% With (TPV 750 mg plus RTV 200 mg) Twice Daily: • ↔ EFV and TPV	With (TPV 500 mg plus RTV 200 mg) Twice Daily: • ETR AUC ↓ 76% and C _{min} ↓ 82% • ↔ TPV AUC and C _{min} ↑ 24%	With (TPV 250 mg plus RTV 200 mg) Twice Daily or with (TPV 750 mg plus RTV 100 mg) Twice Daily: • ↔ NVP • ↔ TPV expected	↑ RPV possible ↔ TPV expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.	No dose adjustment needed.

^a DRV concentration was compared to a historic control.

^b Use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg.

Key to Symbols: ↑ = increase ↓ = decrease ↔ = no change

Key: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; FDA = Food and Drug Administration; FPV = fosamprenavir; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	PK Data	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C _{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	PK Data	↓ BIC expected	With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C _{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	With RAL 400 mg Twice Daily: • RAL AUC ↓ 36% and C _{min} ↓ 21% With RAL 1,200 mg Once Daily: • ↔ RAL AUC and C _{min}
	Dose	Do not coadminister.	In Patients Without INSTI Resistance: • DTG 50 mg twice daily In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance: • Consider alternative combination.	Do not coadminister.	No dose adjustment needed.
ETR	PK Data	↓ BIC expected	ETR 200 mg Twice Daily plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C _{min} ↓ 88% ETR 200 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C _{min} ↓ 37% ETR 200 mg Twice Daily with (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C _{min} ↑ 28%	↑ or ↓ EVG, COBI, and ETR possible	ETR 200 mg Twice Daily plus RAL 400 mg Twice Daily: • ETR C _{min} ↑ 17% • RAL C _{min} ↓ 34%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs, continued					
ETR	Dose	Do not coadminister.	Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r. In Patients Without INSTI Resistance: • DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) In Patients With Certain INSTI-Associated Resistance ^a or Clinically Suspected INSTI Resistance: • DTG 50 mg twice daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	Do not coadminister.	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily is not recommended.
NVP	PK Data	↓ BIC expected	With DTG 50 mg Once Daily: • DTG AUC ↓ 19% and C _{min} ↓ 34%	↑ or ↓ EVG, COBI, and NVP possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
RPV	PK Data	No data	With DTG 50 mg Once Daily: • ↔ DTG AUC and C _{min} ↑ 22% • ↔ RPV AUC and C _{min} ↑ 21%	↑ or ↓ EVG, COBI, and RPV possible	↔ RPV RAL C _{min} ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
PIs					
ATV	PK Data	ATV 400 mg Once Daily plus BIC 75 mg Single Dose: • BIC AUC ↑ 315%	(ATV 400 mg plus DTG 30 mg) Once Daily: • DTG AUC ↑ 91% and C _{min} ↑ 180%	↑ or ↓ EVG, COBI, and ATV possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
ATV/r	PK Data	↑ BIC expected	(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily: • DTG AUC ↑ 62% and C _{min} ↑ 121%	Not applicable	With Unboosted ATV: • RAL AUC ↑ 72% With Unboosted ATV and RAL 1,200 mg: • RAL AUC ↑ 67% With (ATV 300 mg plus RTV 100 mg) Once Daily: • RAL AUC ↑ 41%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
DRV	PK Data	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	Do not administer DRV without RTV or COBI.	Do not administer DRV without RTV or COBI.	No dose adjustment needed.	Do not administer DRV without RTV or COBI.
DRV/c	PK Data	BIC AUC ↑ 74%	DRV/c plus DTG Once Daily: • ↔ DTG, DRV, and COBI DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c: • DTG C _{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
DRV/r	PK Data	No data	(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily: • DTG AUC ↓ 22% and C _{min} ↓ 38%	Not applicable	With (DRV 600 mg plus RTV 100 mg) Twice Daily: • RAL AUC ↓ 29% and C _{min} ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
LPV/r	PK Data	No data	With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily: • ↔ DTG	Not applicable	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
TPV/r	PK Data	↓ BIC possible	With (TPV 500 mg plus RTV 200 mg) Twice Daily and DTG 50 mg Once Daily: • DTG AUC ↓ 59% and C _{min} ↓ 76%	Not applicable	With (TPV 500 mg plus RTV 200 mg) Twice Daily and RAL 400 mg Twice Daily: • RAL AUC ↓ 24% and C _{min} ↓ 55%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 4)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
TPV/r	Dose	Do not coadminister.	In Patients Without INSTI Resistance: <ul style="list-style-type: none"> • DTG 50 mg twice daily In Patients With Certain INSTI-Associated Resistance^a or Clinically Suspected INSTI Resistance: <ul style="list-style-type: none"> • Consider alternative combination. 	Do not coadminister RTV and COBI.	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily is not recommended.

^a Refer to DTG product label for details.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Appendix B, Table 1. Coformulated Single-Tablet Regimens (Last updated July 10, 2019; last reviewed December 18, 2019)

The following table includes dose recommendations for FDA-approved STR products. Please see the class-specific drug characteristics tables ([Appendix B, Tables 3 to 6](#)) for details about the individual drugs included in these STR products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The STR products in this table are listed by drug class and arranged in **alphabetical order** by trade name within each class.

Trade Name (Abbreviations)	ARV Drugs Included in the STR	Dosing Recommendation ^a
INSTI plus Two NRTIs		
Biktarvy (BIC/TAF/FTC)	Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet once daily
Genvoya (EVG/c/TAF/FTC)	Elvitegravir 150 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/emtricitabine 200 mg	One tablet once daily with food
Stribild (EVG/c/TDF/FTC)	Elvitegravir 150 mg/cobicistat 150 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet once daily with food
Triumeq (DTG/ABC/3TC)	Dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg	One tablet once daily
INSTI plus One NRTI		
Dovato (DTG/3TC)	Dolutegravir 50 mg/lamivudine 300 mg	One tablet once daily
PI plus Two NRTIs		
Symtuza (DRV/c/TAF/FTC)	Darunavir 800 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/emtricitabine 200 mg	One tablet once daily with food
NNRTI plus Two NRTIs		
Atripla (EFV/TDF/FTC)	Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet once daily on an empty stomach, preferably at bedtime
Complera (RPV/TDF/FTC)	Rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet once daily with a meal
Delstrigo (DOR/TDF/3TC)	Doravirine 100 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily
Odefsey (RPV/TAF/FTC)	Rilpivirine 25 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet once daily with a meal
Symfi (EFV/TDF/3TC)	Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily on an empty stomach, preferably at bedtime
Symfi Lo (EFV/TDF/3TC)	Efavirenz 400 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily on an empty stomach, preferably at bedtime
INSTI plus One NNRTI		
Juluca (DTG/RPV)	Dolutegravir 50 mg/rilpivirine 25 mg	One tablet once daily with a meal

^a For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 10](#). When no food restriction is listed, the STR can be taken with or without food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 2. Nucleoside Reverse Transcriptase Inhibitor-Based, Fixed-Dose Combination Tablets for Use as Part of an Antiretroviral Regimen (Last updated July 10, 2019; last reviewed December 18, 2019)

The following table includes dose recommendations for FDA-approved, dual-NRTI FDC products. These FDC tablets **are not complete regimens** and must be administered in combination with other ARV drugs.

Please see the class-specific drug characteristics tables ([Appendix B, Tables 3 to 6](#)) for details about the individual drugs contained in these FDC products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The FDC tablets in this table are listed by trade name.

Trade Name (Abbreviations)	ARV Drugs Included in the FDC Tablet	Dosing Recommendation ^a
TAF or TDF plus an NRTI		
Descovy (TAF/FTC)	Tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet once daily
Cimduo (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily
Temixys (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily
Truvada (TDF/FTC)	Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet once daily
Other NRTI-Based, FDC Tablets		
Epzicom (ABC/3TC) Note: Generic product is available.	Abacavir 600 mg/lamivudine 300 mg	One tablet once daily
Combivir (ZDV/3TC) Note: Generic product is available.	Zidovudine 300 mg/lamivudine 150 mg	One tablet twice daily

^a For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 10](#). All FDC tablets listed in this table can be taken without regard to food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

The older NRTIs ddI and d4T are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019, version of the guidelines (found in the archived guidelines section of [AIDSinfo](#)) or to the FDA product labels for ddI and d4T for information regarding these drugs.

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events ^b
Abacavir (ABC) <i>Ziagen</i> Note: Generic tablet formulation is available.	Ziagen: <ul style="list-style-type: none"> • 300 mg tablet • 20 mg/mL oral solution Generic: <ul style="list-style-type: none"> • 300 mg tablet • Also available as FDC with 3TC and ZDV/3TC FDC Tablets that Contain ABC:^c <ul style="list-style-type: none"> • Epzicom (ABC/3TC) • Trizivir (ABC/ZDV/3TC) STRs that Contain ABC:^d <ul style="list-style-type: none"> • Triumeq (DTG/ABC/3TC) 	Ziagen: <ul style="list-style-type: none"> • ABC 600 mg once daily, <i>or</i> • ABC 300 mg twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain ABC.	Metabolized by alcohol dehydrogenase and glucuronyl transferase 82% of ABC dose is excreted renally as metabolites Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	1.5 hours/12–26 hours	Patients who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For patients with a history of HSRs, rechallenge is not recommended . Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath). Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.
Emtricitabine (FTC) <i>Emtriva</i>	Emtriva: <ul style="list-style-type: none"> • 200 mg hard gelatin capsule • 10 mg/mL oral solution FDC Tablets that Contain FTC:^c <ul style="list-style-type: none"> • Descovy (TAF/FTC) • Truvada (TDF/FTC) STRs that Contain FTC:^d <ul style="list-style-type: none"> • Atripla (EFV/TDF/FTC) • Biktarvy (BIC/TAF/FTC) • Complera (RPV/TDF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Stribild (EVG/c/TDF/FTC) • Symtuza (DRV/c/TAF/FTC) 	Emtriva <i>Capsule:</i> <ul style="list-style-type: none"> • FTC 200 mg once daily <i>Oral Solution:</i> <ul style="list-style-type: none"> • FTC 240 mg (24 mL) once daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.	86% of FTC dose is excreted renally See Appendix B, Table 10 for dosing recommendations in patients with renal insufficiency.	10 hours/>20 hours	Minimal toxicity Hyperpigmentation/skin discoloration Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue FTC.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 4)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events ^b
Lamivudine (3TC) <i>Epivir</i> Note: Generic products are available.	Epivir: <ul style="list-style-type: none"> • 150 and 300 mg tablets • 10 mg/mL oral solution Generic: <ul style="list-style-type: none"> • 150 and 300 mg tablets • Also available as FDC with ABC and ZDV FDC Tablets that Contain 3TC:^c <ul style="list-style-type: none"> • Cimduo (TDF/3TC) • Combivir (ZDV/3TC) • Epzicom (ABC/3TC) • Temixys (TDF/3TC) • Trizivir (ABC/ZDV/3TC) STRs that Contain 3TC:^d <ul style="list-style-type: none"> • Delstrigo (DOR/TDF/3TC) • Dovato (DTG/3TC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC) • Trumeq (DTG/ABC/3TC) 	Epivir: <ul style="list-style-type: none"> • 3TC 300 mg once daily, or • 3TC 150 mg twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain 3TC.	70% of 3TC dose is excreted renally See Appendix B, Table 10 for dose recommendations in patients with renal insufficiency.	5–7 hours/18–22 hours	Minimal toxicity Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue 3TC.
Tenofovir Alafenamide (TAF) <i>Vemlidy</i> Note: Vemlidy is available as a 25-mg tablet for the treatment of HBV.	FDC Tablets that Contain TAF:^c <ul style="list-style-type: none"> • Descovy (TAF/FTC) STRs that Contain TAF:^d <ul style="list-style-type: none"> • Biktarvy (BIC/TAF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Symtuza (DRV/c/TAF/FTC) 	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TAF.	Metabolized by cathepsin A. See Appendix B, Table 10 for dosing recommendations in patients with renal insufficiency.	0.5 hours/150–180 hours	Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decreases in BMD are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events ^b
Tenofovir Disoproxil Fumarate (TDF) <i>Viread</i> Note: Generic product is available.	Viread: <ul style="list-style-type: none"> • 150, 200, 250, and 300 mg tablets • 40 mg/g oral powder Generic: <ul style="list-style-type: none"> • 300 mg tablet FDC Tablets that Contain TDF:^c <ul style="list-style-type: none"> • Cimduo (TDF/3TC) • Temixys (TDF/3TC) • Truvada (TDF/FTC) STRs that Contain TDF:^d <ul style="list-style-type: none"> • Atripla (EFV/TDF/FTC) • Complera (RPV/TDF/FTC) • Delstrigo (DOR/TDF/3TC) • Stribild (EVG/c/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC) 	Viread: <ul style="list-style-type: none"> • TDF 300 mg once daily, <i>or</i> • 7.5 level scoops of oral powder once daily (dosing scoop dispensed with each bottle; one level scoop contains 1 g of oral powder). <p>Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt). Do not mix oral powder with liquid.</p> <p>See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.</p>	<p>Renal excretion is the primary route of elimination.</p> <p>See Appendix B, Table 10 for dose recommendations in patients with renal insufficiency.</p>	<p>17 hours/>60 hours</p>	<p>Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy</p> <p>Osteomalacia, decrease in BMD</p> <p>Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TDF.</p> <p>Asthenia, headache, diarrhea, nausea, vomiting, flatulence</p>
Zidovudine (ZDV) <i>Retrovir</i> Note: Generic products are available.	Retrovir: <ul style="list-style-type: none"> • 100 mg capsule • 10 mg/mL IV solution • 10 mg/mL oral solution Generic: <ul style="list-style-type: none"> • 300 mg tablet <p>Also available as FDC with 3TC and 3TC/ABC</p> FDC Tablets that Contain ZDV:^c <ul style="list-style-type: none"> • Combivir (ZDV/3TC) • Trizivir (ABC/ZDV/3TC) 	Retrovir: <ul style="list-style-type: none"> • ZDV 300 mg twice daily, <i>or</i> • ZDV 200 mg three times a day <p>See Appendix B, Table 2 for dosing information for FDC tablets that contain ZDV.</p>	<p>Metabolized to GAZT</p> <p>Renal excretion of GAZT</p> <p>See Appendix B, Table 10 for dosing recommendations in patients with renal insufficiency.</p>	<p>1.1 hours/ 7 hours</p>	<p>Macrocytic anemia</p> <p>Neutropenia</p> <p>Nausea, vomiting, headache, insomnia, asthenia</p> <p>Nail pigmentation</p> <p>Lactic acidosis/severe hepatomegaly with hepatic steatosis (this is a rare, but potentially life-threatening, toxicity)</p> <p>Hyperlipidemia</p> <p>Insulin resistance/diabetes mellitus</p> <p>Lipoatrophy</p> <p>Myopathy</p>

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 4)

^a For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 10](#). When no food restriction is listed, the ARV drug can be taken with or without food.

^b Also see [Table 17](#).

^c See [Appendix B, Table 2](#) for information about these formulations.

^d See [Appendix B, Table 1](#) for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; BMD = bone mineral density; CrCl = creatinine clearance; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FDA = Food and Drug Administration; FTC = emtricitabine; GAZT = azidothymidine glucuronide; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IV = intravenous; MI = myocardial infarction; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; WHO = World Health Organization; ZDV = zidovudine

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

The older NNRTI DLV is no longer commonly used in clinical practice and is **not** listed in this table. Please refer to the FDA product label for DLV for information regarding this drug.

Generic Name (Abbreviations) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/Metabolic Pathway	Serum Half- Life	Adverse Events ^b
Doravirine (DOR) <i>Pifeltro</i>	Pifeltro: • 100 mg tablet Also available as part of the STR Delstrigo (DOR/TDF/3TC) ^c	Pifeltro: • One tablet once daily See Appendix B, Table 1 for dosing information for Delstrigo.	CYP3A4/5 substrate	15 hours	Nausea Dizziness Abnormal dreams
Efavirenz (EFV) <i>Sustiva</i> Note: Generic product is available.	Sustiva: • 50 and 200 mg capsules • 600 mg tablet Generic: • 600 mg tablet STRs that Contain EFV: ^c • Atripla (EFV/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	Sustiva: • EFV 600 mg once daily, at or before bedtime Take on an empty stomach to reduce side effects. See Appendix B, Table 1 for dosing information for STRs that contain EFV.	Metabolized by CYP2B6 (primary), 3A4, and 2A6 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2B6 and 2C19 inducer	40–55 hours	Rash ^d Neuropsychiatric symptoms ^e Serum transaminase elevations Hyperlipidemia Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays. QT interval prolongation
Etravirine (ETR) <i>Intence</i>	Intence: • 25, 100, and 200 mg tablets	Intence: • ETR 200 mg twice daily Take following a meal.	CYP3A4, 2C9, and 2C19 substrate CYP3A4 inducer CYP2C9 and 2C19 inhibitor	41 hours	Rash, including Stevens-Johnson syndrome ^d HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported. Nausea

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 2)

Generic Name (Abbreviations) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/Metabolic Pathway	Serum Half- Life	Adverse Events ^b
Nevirapine (NVP) <i>Viramune or Viramune XR</i> Note: Generic products are available.	Viramune: <ul style="list-style-type: none"> • 200 mg tablet • 50 mg/5 mL oral suspension Viramune XR: <ul style="list-style-type: none"> • 400 mg tablet Generic: <ul style="list-style-type: none"> • 200 mg tablet • 400 mg extended release tablet • 50 mg/5 mL oral suspension 	Viramune: <ul style="list-style-type: none"> • NVP 200 mg once daily for 14 days (lead-in period); thereafter, NVP 200 mg twice daily, or • NVP 400 mg (Viramune XR tablet) once daily Take without regard to meals. Repeat lead-in period if therapy is discontinued for >7 days. In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in dose until rash resolves, but do not extend lead-in period beyond 28 days total.	CYP450 substrate CYP3A4 and 2B6 inducer Contraindicated in patients with moderate to severe hepatic impairment. Dose adjustment is recommended in patients on hemodialysis (see Appendix B, Table 10).	25–30 hours	Rash, including Stevens-Johnson syndrome ^d Symptomatic Hepatitis: <ul style="list-style-type: none"> • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported. • Rash has been reported in approximately 50% of cases. • Symptomatic hepatitis occurs at a significantly higher frequency in ARV-naïve female patients with pre-NVP CD4 counts >250 cells/mm³ and in ARV-naïve male patients with pre-NVP CD4 counts >400 cells/mm³. • NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.
Rilpivirine (RPV) <i>Edurant</i>	Edurant: <ul style="list-style-type: none"> • 25 mg tablet STRs that Contain RPV:^c <ul style="list-style-type: none"> • Complera (RPV/TDF/FTC) • Juluca (DTG/RPV) • Odefsey (RPV/TAF/FTC) 	Edurant: <ul style="list-style-type: none"> • RPV 25 mg once daily Take with a meal. See Appendix B, Table 1 for dosing information for STRs that contain RPV.	CYP3A4 substrate	50 hours	Rash ^d Depression, insomnia, headache Hepatotoxicity QT interval prolongation

^a For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 10](#). When no food restriction is listed, the ARV drug can be taken with or without food.

^b Also see [Table 17](#).

^c See [Appendix B, Table 1](#) for information about these formulations.

^d Rare cases of Stevens-Johnson syndrome have been reported with the use of most NNRTIs; the highest incidence of rash was seen among patients who were receiving NVP.

^e Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, depression, suicidality (e.g., suicide, suicide attempt or ideation), confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of patients who are receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but discontinuation of EFV may be necessary in a small percentage of patients. **Late-onset neurotoxicities, including ataxia and encephalopathy, have been reported.**

Key: 3TC = lamivudine; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DLV = delavirdine; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FDC = fixed-dose combination; FTC = emtricitabine; HSR = hypersensitivity reaction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

The older PIs FPV, IDV, NFV, SQV, and TPV are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019 version of the guidelines (found in the archived guidelines section of *AIDSinfo*) or to the FDA product labels for information regarding these drugs.

Generic Name (Abbreviations) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events ^b
Atazanavir (ATV) <i>Reyataz</i> (ATV/c) <i>Evotaz</i> Note: Generic products of ATV are available.	Reyataz: <ul style="list-style-type: none"> • 150, 200, and 300 mg capsules • 50 mg oral powder/packet Generic: <ul style="list-style-type: none"> • 100, 150, 200, and 300 mg capsules Evotaz: <ul style="list-style-type: none"> • ATV 300 mg/COBI 150 mg tablet 	Reyataz <i>In ARV-Naive Patients:</i> <ul style="list-style-type: none"> • (ATV 300 mg plus RTV 100 mg) once daily; or • ATV 400 mg once daily • Take with food. <i>With TDF or in ARV-Experienced Patients:</i> <ul style="list-style-type: none"> • (ATV 300 mg plus RTV 100 mg) once daily • Unboosted ATV is not recommended. • Take with food. <i>With EFV in ARV-Naive Patients:</i> <ul style="list-style-type: none"> • (ATV 400 mg plus RTV 100 mg) once daily • Take with food. Evotaz: <ul style="list-style-type: none"> • One tablet once daily • Take with food. • The use of ATV/c is not recommended for patients who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). For dosing recommendations for patients who are also receiving H2 antagonists and PPIs, refer to Table 21a .	ATV: <ul style="list-style-type: none"> • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor COBI: <ul style="list-style-type: none"> • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7 hours	Indirect hyperbilirubinemia PR interval prolongation. First degree symptomatic AV block has been reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation. Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when ATV is administered with COBI.

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 4)

Generic Name (Abbreviations) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events ^b
Darunavir (DRV) <i>Prezista</i> (DRV/c) <i>Prezcobix</i>	Prezista: <ul style="list-style-type: none"> • 75, 150, 600, and 800 mg tablets • 100 mg/mL oral suspension Prezcobix: <ul style="list-style-type: none"> • DRV 800 mg/ COBI 150 mg tablet <p>Also available as part of the STR Symtuza (DRV/c/ TAF/FTC)</p>	Prezista <i>In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:</i> <ul style="list-style-type: none"> • (DRV 800 mg plus RTV 100 mg) once daily • Take with food. <i>In ARV-Experienced Patients with One or More DRV Resistance Mutations:</i> <ul style="list-style-type: none"> • (DRV 600 mg plus RTV 100 mg) twice daily • Take with food. <p>Unboosted DRV is not recommended.</p> Prezcobix: <ul style="list-style-type: none"> • One tablet once daily • Take with food. • Not recommended for patients with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF is not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). <p>See Appendix B, Table 1 for dosing information for Symtuza.</p>	DRV: <ul style="list-style-type: none"> • CYP3A4 inhibitor and substrate • CYP2C9 inducer COBI: <ul style="list-style-type: none"> • CYP3A inhibitor and substrate • CYP2D6 inhibitor 	15 hours when combined with RTV 7 hours when combined with COBI	Skin Rash: DRV has a sulfonamide moiety, however incidence and severity of rash are similar in those with or without a sulfonamide allergy; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported. Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when DRV is administered with COBI.

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

Generic Name (Abbreviations) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events ^b
Lopinavir/ Ritonavir (LPV/r) <i>Kaletra</i> Note: LPV is only available as a component of an FDC tablet that also contains RTV.	Kaletra: <ul style="list-style-type: none"> • LPV/r 200 mg/50 mg tablets • LPV/r 100 mg/25 mg tablets • LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol. 	Kaletra: <ul style="list-style-type: none"> • LPV/r 400 mg/100 mg twice daily, <i>or</i> • LPV/r 800 mg/200 mg once daily. However, once-daily dosing is not recommended for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, carbamazepine, phenytoin, or phenobarbital. <i>With EFV or NVP in PI-Naive or PI Experienced Patients:</i> <ul style="list-style-type: none"> • LPV/r 500 mg/125 mg tablets twice daily (use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg), <i>or</i> • LPV/r 533 mg/133 mg oral solution twice daily Food Restrictions <i>Tablet:</i> <ul style="list-style-type: none"> • Take without regard to meals. <i>Oral Solution:</i> <ul style="list-style-type: none"> • Take with food. 	CYP3A4 inhibitor and substrate	5–6 hours	GI intolerance, nausea, vomiting, diarrhea Pancreatitis Asthenia Hyperlipidemia (especially hypertriglyceridemia) Serum transaminase elevation Hyperglycemia Insulin resistance/diabetes mellitus Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia PR interval prolongation QT interval prolongation and Torsades de Pointes have been reported; however, causality could not be established.
Ritonavir (RTV) Norvir Note: Generic is available. Although RTV was initially developed as a PI for HIV treatment, RTV is currently used at a lower dose of 100 mg to 200 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	Norvir: <ul style="list-style-type: none"> • 100 mg tablet • 100 mg soft gel capsule • 80 mg/mL oral solution. Oral solution contains 43% alcohol. • 100 mg single packet oral powder Also available as part of the FDC tablet Kaletra (LPV/r)	As a PK Booster (or Enhancer) for Other PIs: <ul style="list-style-type: none"> • RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations). Food Restrictions <i>Tablet:</i> <ul style="list-style-type: none"> • Take with food. <i>Capsule and Oral Solution:</i> <ul style="list-style-type: none"> • To improve tolerability, take with food if possible. 	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Taste perversion Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 4)

^a For dose adjustments in patients with hepatic insufficiency, see [Appendix B, Table 10](#).

^b Also see [Table 17](#).

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDA = Food and Drug Administration; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFV = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronyl transferase

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathways	Serum Half- Life	Adverse Events ^b
Bictegravir (BIC)	BIC is only available as a component of the STR Biktarvy (BIC/TAF/FTC). ^c	Biktarvy: • One tablet PO once daily	CYP3A4 substrate UGT1A1-mediated glucuronidation	~17 hours	Diarrhea Nausea Headache Weight gain
Dolutegravir (DTG) <i>Tivicay</i>	Tivicay: • 50 mg tablet STRs that Contain DTG: ^c • Dovato (DTG/3TC) • Juluca (DTG/RPV) • Trumeq (DTG/ABC/3TC)	In ARV-Naive or ARV-Experienced, INSTI-Naive Patients: • DTG 50 mg PO once daily In ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin: • DTG 50 PO mg twice daily INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance: • DTG 50 mg PO twice daily See Appendix B, Table 1 for dosing information for STRs that contain DTG.	UGT1A1-mediated glucuronidation Minor substrate of CYP3A4	~14 hours	Insomnia Headache Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions) Weight gain Hepatotoxicity There is a potential increased risk of NTDs in infants born to individuals who received DTG around the time of conception (see Table 6b for more information). HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.
Elvitegravir (EVG)	EVG is only available as a component of an STR tablet that also contains COBI, FTC, and either TDF or TAF. STRs that Contain EVG: ^c • Genvoya (EVG/c/TAF/FTC) • Stribild (EVG/c/TDF/FTC)	Genvoya: • One tablet PO once daily with food • See Appendix B, Table 10 for recommendations on dosing in persons with renal insufficiency. Stribild: • One tablet PO once daily with food • Not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the CrCl calculation equation).	EVG: • CYP3A and UGT1A1/3 substrate COBI: • CYP3A inhibitor and substrate • CYP2D6 inhibitor	EVG/c: ~13 hours	Nausea Diarrhea Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions)

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 2)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations ^a	Elimination/ Metabolic Pathways	Serum Half- Life	Adverse Events ^b
Raltegravir (RAL) <i>Isentress</i> <i>Isentress HD</i>	Isentress: <ul style="list-style-type: none"> • 400 mg tablet • 25 and 100 mg chewable tablets • 100 mg single-use packet for oral suspension Isentress HD: <ul style="list-style-type: none"> • 600 mg tablet 	Isentress <i>In ARV-Naive Patients or ARV-Experienced Patients:</i> <ul style="list-style-type: none"> • 400 mg PO twice daily <i>With Rifampin:</i> <ul style="list-style-type: none"> • 800 mg twice daily Isentress HD <i>In ARV-Naive or ARV-Experienced Patients with Virologic Suppression on a Regimen containing RAL 400 mg Twice Daily:</i> <ul style="list-style-type: none"> • 1,200 mg (two 600-mg tablets) PO once daily <i>With Rifampin:</i> <ul style="list-style-type: none"> • Not recommended 	UGT1A1-mediated glucuronidation	~9 hours	Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis Nausea Headache Diarrhea Pyrexia CPK elevation, muscle weakness, and rhabdomyolysis Weight gain Insomnia Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions)

^a For dose adjustments in patients with hepatic insufficiency, see [Appendix B, Table 10](#). When no food restriction is listed, the ARV drug can be taken with or without food.

^b Also see [Table 17](#).

^c See [Appendix B, Table 1](#) for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; COBI = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; PO = orally; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate glucuronyl transferase

Appendix B, Table 7. Characteristics of the Fusion Inhibitor (Last updated December 18, 2019; last reviewed December 18, 2019)

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendation	Serum Half- Life	Elimination	Adverse Events ^a
Enfuvirtide (T-20) <i>Fuzeon</i>	Fuzeon: <ul style="list-style-type: none"> • Injectable; supplied as lyophilized powder. • Each vial contains 108 mg of T-20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL. • Refer to prescribing information for storage instruction. 	Fuzeon: <ul style="list-style-type: none"> • T-20 90 mg/1 mL SQ twice daily 	3.8 hours	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool	Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) in almost 100% of patients Increased incidence of bacterial pneumonia HSR occurs in <1% of patients. Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. Re-challenge is not recommended.

^a Also see [Table 17](#).

Key: HSR = hypersensitivity reaction; SQ = subcutaneous; T-20 = enfuvirtide

Appendix B, Table 8. Characteristics of the CCR5 Antagonist (Last updated December 18, 2019; last reviewed December 18, 2019)

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations ^a	Serum Half-Life	Elimination/Metabolic Pathway	Adverse Events ^b
Maraviroc (MVC) <i>Selzentry</i>	Selzentry: • 150 and 300 mg tablets	Selzentry: • MVC 150 mg PO twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r) • MVC 300 mg PO twice daily when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • MVC 600 mg PO twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC without regard to meals.	14–18 hours	CYP3A4 substrate	Abdominal pain Cough Dizziness Musculoskeletal symptoms Pyrexia Rash Upper respiratory tract infections Hepatotoxicity, which may be preceded by severe rash or other signs of systemic allergic reactions Orthostatic hypotension, especially in patients with severe renal insufficiency

^a For dose adjustments in patients with hepatic insufficiency, see [Appendix B, Table 10](#).

^b Also see [Table 17](#).

Key: CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; T-20 = enfuvirtide; TPV/r = tipranavir/ritonavir

Appendix B, Table 9. Characteristics of the CD4 Post-Attachment Inhibitor (Last updated December 18, 2019; last reviewed December 18, 2019)

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events
Ibalizumab (IBA) <i>Trogarzo</i>	Trogarzo: • Single-dose 2 mL vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab	Trogarzo: • Administer a single loading dose of IBA 2,000 mg IV infusion over 30 minutes, followed by a maintenance dose of IBA 800 mg IV infusion over 15 minutes every 2 weeks. • See prescribing information for additional instructions for preparing, storing, and administering IBA, and for monitoring patients who are receiving IBA.	~64 hours	Not well defined	Diarrhea Dizziness Nausea Rash

Key: IBA = ibalizumab; IV = intravenous

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 6)

The older ARV drugs ddI, d4T, FPV, IDV, NFV, SQV, and TPV are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019, guidelines in the Guidelines Archive section of *AIDSinfo* or to the FDA product labels for these drugs for recommendations on dosing in persons with renal or hepatic insufficiency.

See the reference section at the end of this table for CrCl calculation formulas and criteria for Child-Pugh classification.

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
<p>Some FDC products are not recommended in persons with different degrees of renal insufficiency. The recommendations for individual FDCs based on CrCl level are outlined below.</p> <ul style="list-style-type: none"> • CrCl <70 mL/min: Initiation of Stribild is not recommended. • CrCl <50 mL/min: FDCs not recommended: Atripla, Combivir, Complera, Delstrigo, Dovato, Epzicom, Trisun, or Trizivir. • CrCl <30 mL/min: FDCs not recommended: Biktarvy and Truvada. • CrCl <30 mL/min and not on HD: FDCs not recommended: Descovy, Genvoya, Odefsey, and Symtuza. <p>The component drugs in some of the FDC products listed above may be prescribed as individual formulations with dose adjustment based on CrCl level as indicated below in this table.</p>			
NRTIs			
Abacavir (ABC) <i>Ziagen</i>	ABC 300 mg PO twice daily or ABC 600 mg PO once daily	No dose adjustment necessary.	<i>Child-Pugh Class A:</i> ABC 200 mg PO twice daily (use oral solution) <i>Child-Pugh Class B or C:</i> Contraindicated
Emtricitabine (FTC) <i>Emtriva</i>	FTC 200 mg oral capsule once daily or FTC 240 mg (24 mL) oral solution once daily	Dose by Formulation	
		CrCl (mL/min)	Capsule
		30–49	200 mg every 48 hours
		15–29	200 mg every 72 hours
		<15	200 mg every 96 hours
Lamivudine (3TC) <i>Epivir</i>	3TC 300 mg PO once daily or 3TC 150 mg PO twice daily	Dose	
		30–49	150 mg every 24 hours
		15–29	1 x 150 mg, then 100 mg every 24 hours
		5–14	1 x 150 mg, then 50 mg every 24 hours
		<5 or on HD ^b	1 x 50 mg, then 25 mg every 24 hours
Tenofovir Alafenamide (TAF) <i>Vemlidy</i>	Vemlidy is available as a 25-mg tablet for the treatment of HBV.	CrCl (mL/min)	Dose
		<15 and not on HD	Not recommended
		On HD ^b	One tablet once daily.

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 6)

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency		Dosing in Persons with Hepatic Impairment
NRTIs, continued				
Tenofovir Alafenamide/ Emtricitabine (TAF/FTC) Descovy	TAF for HIV treatment is only available as a component of FDC tablets (i.e., in Descovy, Genvoya, Odefsey, Biktarvy, and Symtuza). TAF 10 mg PO daily with EVG/c (Genvoya) or DRV/c (Symtuza) TAF 25 mg PO daily in other FDC tablets	CrCl (mL/min)	Dose	Child-Pugh Class A or B: No dose adjustment Child-Pugh Class C: No dose recommendation
		<30 and not on HD	Not recommended	
		<30 and on HD ^b	One tablet once daily.	
Tenofovir Disoproxil Fumarate (TDF) Viread	TDF 300 mg PO once daily	CrCl (mL/min)	Dose	No dose adjustment necessary.
		30–49	300 mg every 48 hours	
		10–29	300 mg twice weekly (every 72–96 hours)	
		<10 and not on HD	No recommendation	
		On HD ^b	300 mg every 7 days	
Tenofovir Disoproxil Fumarate/ Emtricitabine (TDF/FTC) Truvada	One tablet PO once daily	CrCl (mL/min)	Dose	No dose recommendation.
		30–49	One tablet every 48 hours	
		<30 or on HD	Not recommended	
Tenofovir Disoproxil Fumarate/Lamivudine (TDF/3TC) Cimduo	One tablet PO once daily	CrCl (mL/min)	Dose	No dose recommendation.
		<50 or on HD	Not recommended	
Zidovudine (ZDV) Retrovir	ZDV 300 mg PO twice daily	CrCl (mL/min)	Dose	No dose recommendation.
		<15 or on HD ^b	100 mg three times a day or 300 mg once daily	
NNRTIs				
Doravirine (DOR) Pifeltro	One tablet PO once daily	No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in individuals with ESRD or on HD.		Child-Pugh Class A or B: No dose adjustment
				Child-Pugh Class C: Not studied
Doravirine/Tenofovir Disoproxil Fumarate/ Lamivudine (DOR/TDF/3TC) Delstrigo	One tablet PO once daily	Not recommended if CrCl <50 mL/min.		Child-Pugh Class A or B: No dose adjustment
				Child-Pugh Class C: Not studied

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 6)

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
NNRTIs, continued			
Efavirenz (EFV) <i>Sustiva</i>	EFV 600 mg PO once daily on an empty stomach, preferably at bedtime	No dose adjustment necessary.	No dose recommendation; use with caution in patients with hepatic impairment.
Efavirenz/Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC) <i>Atripla</i>	One tablet PO once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min. Instead, use the individual component ARVs and adjust TDF and FTC doses according to CrCl level.	No dose recommendation; use with caution in patients with hepatic impairment.
Efavirenz 600 mg/ Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC) <i>Symfi</i>	One tablet once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min or if patient is on HD. Instead, use the individual component ARVs and adjust TDF and 3TC doses according to CrCl level.	Not recommended for patients with moderate or severe hepatic impairment. Use with caution in patients with mild hepatic impairment.
Efavirenz 400 mg/ Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC) <i>Symfi Lo</i>	One tablet once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min or if patient is on HD. Instead, use the individual component ARVs and adjust TDF and 3TC doses according to CrCl level.	Not recommended for patients with moderate or severe hepatic impairment. Use with caution in patients with mild hepatic impairment.
Etravirine (ETR) <i>Intence</i>	ETR 200 mg PO twice daily	No dose adjustment necessary.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation
Nevirapine (NVP) <i>Viramune</i> or <i>Viramune XR</i>	NVP 200 mg PO twice daily or NVP 400 mg PO once daily (using Viramune XR formulation)	No dose adjustment for patients with renal impairment. Patients on HD should receive an additional dose of NVP 200 mg following each dialysis treatment.	<i>Child-Pugh Class A:</i> No dose adjustment <i>Child-Pugh Class B or C:</i> Contraindicated
Rilpivirine (RPV) <i>Edurant</i>	RPV 25 mg PO once daily	No dose adjustment necessary.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation
Rilpivirine/Tenofovir Alafenamide/ Emtricitabine (RPV/TAF/FTC) <i>Odefsey</i>	One tablet PO once daily	In Patients on Chronic HD: • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation
Rilpivirine/Tenofovir Disoproxil Fumarate/ Emtricitabine (RPV/TDF/FTC) <i>Complera</i>	One tablet PO once daily	Not recommended if CrCl <50 mL/min. Instead, use the individual component ARVs and adjust TDF and FTC doses according to CrCl level.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 6)

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
NNRTIs, continued			
Rilpivirine/ Dolutegravir (RPV/DTG) <i>Juluca</i>	One tablet PO once daily with food	No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation
PIs			
Atazanavir (ATV) <i>Reyataz</i>	ATV 400 mg PO once daily or (ATV 300 mg plus RTV 100 mg) PO once daily	No dose adjustment for patients with renal dysfunction who do not require HD. In ARV-Naive Patients on HD: • (ATV 300 mg plus RTV 100 mg) once daily In ARV-Experienced Patients on HD: • ATV and ATV/r are not recommended	<i>Child-Pugh Class A:</i> No dose adjustment <i>Child-Pugh Class B:</i> ATV 300 mg once daily (unboosted) for ARV-naive patients only <i>Child-Pugh Class C:</i> Not recommended RTV boosting is not recommended in patients with hepatic impairment.
Atazanavir/Cobicistat (ATV/c) <i>Evotaz</i>	One tablet PO once daily	If Used with TDF: • Not recommended if CrCl <70 mL/min	Not recommended in patients with hepatic impairment.
Darunavir (DRV) <i>Prezista</i>	In ARV-Naive Patients and ARV-Experienced Patients with No DRV Resistance Mutations: • (DRV 800 mg plus RTV 100 mg) PO once daily with food In ARV-Experienced Patients with at Least One DRV Resistance Mutation: • (DRV 600 mg plus RTV 100 mg) PO twice daily	No dose adjustment necessary.	<i>In Patients with Mild-to-Moderate Hepatic Impairment:</i> No dose adjustment <i>In Patients with Severe Hepatic Impairment:</i> Not recommended
Darunavir/Cobicistat (DRV/c) <i>Prezcobix</i>	One tablet PO once daily	If Used with TDF: • Not recommended if CrCl <70 mL/min	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> Not recommended
Darunavir/ Cobicistat/Tenofovir Alafenamide/ Emtricitabine (DRV/c/TAF/FTC) <i>Symtuza</i>	One tablet PO once daily	In Patients on Chronic HD: • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	Not recommended for patients with severe hepatic impairment.

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 6)

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
PIs, continued			
Lopinavir/Ritonavir (LPV/r) <i>Kaletra</i>	(LPV/r 400 mg/100 mg) PO twice daily or (LPV/r 800 mg/200 mg) PO once daily	Avoid once-daily dosing in patients on HD.	No dose recommendation; use with caution in patients with hepatic impairment.
Ritonavir (RTV) <i>Norvir</i>	As a PI-Boosting Agent: • RTV 100–400 mg per day	No dose adjustment necessary.	Refer to recommendations for the primary (i.e., boosted) PI.
INSTIs			
Bictegravir/Tenofovir Alafenamide/ Emtricitabine (BIC/TAF/FTC) <i>Biktarvy</i>	One tablet once daily	Not recommended for use in patients with CrCl <30 mL/min.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C: Not recommended</i>
Dolutegravir (DTG) <i>Tivicay</i>	DTG 50 mg once daily or DTG 50 mg twice daily	No dose adjustment necessary.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C: Not recommended</i>
Dolutegravir/ Abacavir/Lamivudine (DTG/ABC/3TC) <i>Triumeq</i>	One tablet once daily	Not recommended if CrCl <50 mL/min. Instead, use the individual component drugs and adjust 3TC dose according to CrCl.	<i>Child-Pugh Class A:</i> Patients with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these patients. <i>Child-Pugh Class B or C: Contraindicated</i> due to the ABC component
Dolutegravir/ Rilpivirine (DTG/RPV) <i>Juluca</i>	One tablet PO once daily with food	No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects.	<i>Child-Pugh Class A or B:</i> No dose adjustment <i>Child-Pugh Class C:</i> No dose recommendation
Elvitegravir/ Cobicistat/Tenofovir Alafenamide/ Emtricitabine (EVG/c/TAF/FTC) <i>Genvoya</i>	One tablet once daily	In Patients on Chronic HD: • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	<i>In Patients with Mild-to-Moderate Hepatic Insufficiency:</i> No dose adjustment necessary <i>In Patients with Severe Hepatic Insufficiency: Not recommended</i>
Elvitegravir/ Cobicistat/Tenofovir Disoproxil Fumarate/ Emtricitabine (EVG/c/TDF/FTC) <i>Stribild</i>	One tablet once daily	EVG/c/TDF/FTC should not be initiated in patients with CrCl <70 mL/min. Discontinue EVG/c/TDF/FTC if CrCl declines to <50 mL/min while patient is on therapy.	<i>In Patients with Mild-to-Moderate Hepatic Insufficiency:</i> No dose adjustment necessary <i>In Patients with Severe Hepatic Insufficiency: Not recommended</i>

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 6 of 6)

Generic Name (Abbreviations) Trade Name	Usual Daily Dose ^a	Dosing in Persons with Renal Insufficiency	Dosing in Persons with Hepatic Impairment
INSTIs, continued			
Raltegravir (RAL) <i>Isentress</i> <i>Isentress HD</i>	RAL 400 mg twice daily (using Isentress formulation) or RAL 1,200 mg once daily (using Isentress HD formulation only)	No dose adjustment necessary.	<i>In Patients with Mild-to-Moderate Hepatic Insufficiency:</i> No dose adjustment necessary <i>In Patients with Severe Hepatic Insufficiency:</i> No recommendation
Fusion Inhibitor			
Enfuvirtide (T-20) <i>Fuzeon</i>	T-20 90 mg SQ twice daily	No dose adjustment necessary.	No dose adjustment necessary.
CCR5 Antagonist			
Maraviroc (MVC) <i>Selzentry</i>	The recommended dose differs based on concomitant medications and potential for drug-drug interactions. See Appendix B, Table 8 for detailed dosing information.	In Patients with CrCl <30 mL/min or Patients Who Are on HD <i>Without Potent CYP3A Inhibitors or Inducers:</i> • MVC 300 mg twice daily; if postural hypotension occurs, reduce to MVC 150 mg twice daily <i>With Potent CYP3A Inducers or Inhibitors:</i> • Not recommended	No dose recommendations. MVC concentrations will likely be increased in patients with hepatic impairment.
CD4 Post-Attachment Inhibitor			
Ibalizumab (IBA) <i>Trogarzo</i>	Loading dose: IBA 2,000 mg IV Maintenance dose: IBA 800 mg IV every 2 weeks	No dose adjustment recommended.	No recommendation.

^a Refer to [Appendix B, Tables 1–9](#) for additional dosing information.

^b On dialysis days, the patient should take the dose after the HD session.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAPD = chronic ambulatory peritoneal dialysis; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; HBV = hepatitis B virus; HD = hemodialysis; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; XR = extended release; ZDV = zidovudine

Creatinine Clearance Calculation	
Male: $\frac{(140 - \text{age in years}) \times (\text{weight in kg})}{72 \times (\text{serum creatinine})}$	Female: $\frac{(140 - \text{age in years}) \times (\text{weight in kg}) \times (0.85)}{72 \times (\text{serum creatinine})}$

Child-Pugh Score			
Component	Points Scored		
	1	2	3
Encephalopathy ^a	None	Grade 1–2	Grade 3–4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory despite diuretics
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
Total Bilirubin, <i>or</i>	<2 mg/dL (<34 μmol/L)	2–3 mg/dL (34–50 μmol/L)	>3 mg/dL (>50 μmol/L)
Modified Total Bilirubin ^b	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin Time (Seconds Prolonged), <i>or</i>	<4	4–6	>6
International Normalized Ratio (INR)	<1.7	1.7–2.3	>2.3

^a Encephalopathy Grades

Grade 1: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination

Grade 2: Drowsiness, disorientation, asterixis

Grade 3: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation

Grade 4: Coma, decerebrate posturing, flaccidity

^b Modified total bilirubin used for patients who have Gilbert's syndrome or who are taking indinavir or atazanavir.

Child-Pugh Classification	Total Child-Pugh Score ^a
Class A	5–6 points
Class B	7–9 points
Class C	>9 points

^a Sum of points for each component of the Child-Pugh Score.